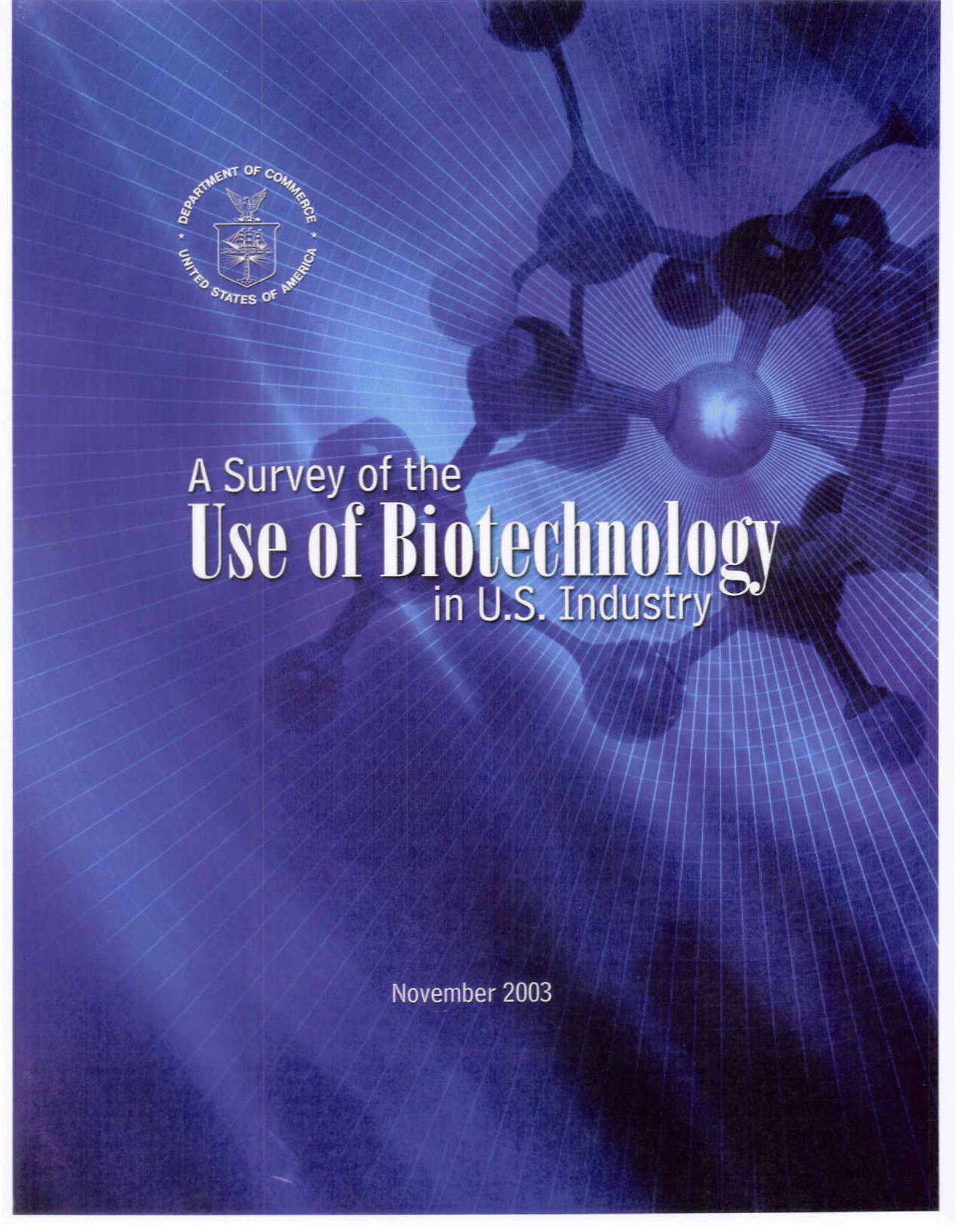

A Survey of the Use of Biotechnology in U.S. Industry

November 2003

Many people worked together on this first federal survey effort examining the use of biotechnology in U.S. industry. Appreciation and thanks to the following individuals from the Department of Commerce Technology Administration (TA), the Economics and Statistics Administration, the Bureau of Industry and Security (BIS), and the International Trade Administration (ITA), as well as the Department of Labor (DOL).

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A SURVEY OF THE USE OF BIOTECHNOLOGY IN U.S. INDUSTRY

U.S. Department of Commerce
Technology Administration
Bureau of Industry & Security
November 2003

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FOREWORD

At the dawn of the 21st century, no new area of science and technology holds greater promise or potential than biotechnology. From genomics and proteomics to biotechnologies for improving industrial production processes, advances in our ability to understand and manipulate living materials promise to address many significant challenges facing our society.

Improving Human Health. Millions of people around the world are already living longer, healthier lives thanks to cures, treatments, and diagnoses made possible through recent advances in biotechnology. Over the next century, further advances in the biosciences promise to improve the health and lives of billions more.

Ending Hunger. Agricultural biotechnologies are significantly increasing crop yields while reducing reliance on chemical herbicides and pesticides. For example, the addition of vitamin A to rice has the potential to save the lives of millions of children in the developing world each year. Similar advances in bio-agriculture will help feed a rapidly growing world with healthier foods.

Meeting Our Energy and Environmental Needs. Biofuels represent an important avenue to reduce dependence on oil and improve the quality of our environment. Also, enzymes identified or designed through biotechnology offer ways to clean up waste while reducing pollution caused by industrial processes or accidents.

Defending Our Homeland. Vaccines, sensors, and biometric devices will be a critical part of our security and authentication infrastructure for homeland defense efforts.

Catalyzing New Innovations. In the longer term, advances in biotechnology promise new technology platforms for the creation of self-healing, self-assembling networks and new materials and processes.

Promoting Economic Growth and Competitiveness. Biotechnology will be essential to national long-term economic growth and leadership. From job creation to revenue generation, strength in biotech will be a core building block of America's national competitiveness in the 21st century.

But to support progress in biotechnology most effectively, policymakers and business leaders require timely and accurate data about the nature and economic impacts of industries that are pioneering biotech's development and adoption. The August 2002 survey, *Critical Technology Assessment of Biotechnology in U.S. Industry*, was the first effort to collect official comprehensive statistics about the use and development of this important technology and its contributions to the U.S. economy.

This analysis of survey data provides information about the current development and adoption of biotechnology in more than 1,000 companies and in various industries and makes a signifi-

cant contribution to future survey efforts. These unique results represent the culmination of more than two years of discussion with biotechnology firms, state agencies and governments, numerous federal agencies, and the Biotechnology Industry Organization (BIO)—the largest U.S. biotechnology association.

The Commerce Department's Office of Technology Policy (OTP) welcomes your comments and suggestions for future surveys, reports, and analyses.

Bruce P. Mehlman
Assistant Secretary for Technology Policy

Executive Summary

In 2002, the U.S. Department of Commerce's Bureau of Industry and Security (BIS), Office of Strategic Industries and Economic Security, and the Technology Administration's Office of Technology Policy (OTP) initiated the first in-depth government assessment of the development and adoption of biotechnology in industry. This assessment was intended to increase national policymakers' understanding of the current development and use of biotechnology in U.S. industries, and to assist federal statistical agencies in developing measures and statistics of biotechnology-related economic activity.

The analysis and findings in this report are largely based on data collected from a survey of more than 3,000 firms engaged in biotechnology-related activities. The findings include the following:

- Firms engaged in biotechnology activities vary greatly in size and scope. They range from small, dedicated biotechnology companies that are R&D-intensive and operate primarily on venture capital, grants, initial public offerings (IPOs) and collaborative agreements, to large, diversified companies that have greater in-house resources and well-established production and distribution systems.

- Larger firms account for the majority of net sales and operating income of businesses with biotech activities, although 90% (917 firms) of survey respondents had 500 or fewer employees. Only 19 firms (2%) reported more than 15,000 employees, while 600 (58%) had fewer than 50.

- Survey respondents that are engaged in biotechnology research, development, and applications reported that in 2001 they had more than 1.1 million employees, total annual net sales of about $567 billion, operating income of $100.5 billion, capital expenditures of $29.5 billion, and R&D expenditures of $ 41.6 billion.

- For 90% of firms, biotech-related business lines accounted for more than 75% of total net sales, employment, and operating income. These companies generally are smaller firms with fewer than 500 employees. For all respondents, biotechnology-related business lines accounted for almost 40% of total R&D expenditures.

- International markets accounted for at least 16% of firms' biotechnology-related net sales or $8 billion in revenues in 2001. The leading foreign market for biotechnology exports is Europe (56% of export revenues), followed by the Asia/Pacific region (24%). Almost one-quarter of companies indicated that they plan to expand into a foreign market as part of their near-term competitive strategy.

- Patent data underscore the dynamic and rapidly evolving nature of biotechnology. In the last quarter of 2002, companies reported 33,131 pending applications for biotechnology products or processes, compared with 23,992 current portfolio patents.

- Seventy percent of respondents were headquartered in ten states, with 26% located in California. Massachusetts, Maryland, Pennsylvania, North Carolina, and New Jersey also had notable concentrations of biotechnology firms.

- Firms indicated that they belonged to more than 60 North American Industry Classification System (NAICS) industry codes. However, more than 65% of all firms classified themselves in one of two NAICS categories—Scientific R&D Services (category 5417) or Pharmaceutical and Medicine Manufacturing (3254).

Industries and Areas of Activity

- Almost three-quarters of firms (72%) indicated that human health (HH) applications are their primary area of biotechnology-related activity. Between 90% and 98% of all biotechnology-related financial activity reported by survey respondents was attributable to the 780 companies that selected HH as a primary or secondary application area.

- The area of greatest concentration for HH firms is therapeutics—some 70% of companies reported a focus in this area. Medical diagnostics and therapeutics were less prominent, with 42% and 21%, respectively, of firms citing activity in these areas. Relatively few firms active in human health currently have approved and marketed products or processes. The most common commercial product/process was diagnostic tests, a category cited by 11% of HH companies.

- For HH firms, biotechnology-related activities accounted for 26% of capital investments and 40% of R&D expenditures, but only 15% of annual net sales and 14% of operating income in 2001.

- Firms also are engaged in other types of biotechnology applications. Between 12% and 14% of respondents indicated that their primary or secondary biotechnology activities were related to animal health, agriculture, or aquaculture/marine (AAM) applications, or industrial and agricultural derived-processing. Four to five percent of companies work in microbial applications or environmental remediation and natural resource recovery.

- Companies that reported a primary or secondary concentration in biotechnology-related AAM activities focus their R&D efforts on seeds and plants (63%), livestock (41%), and aquaculture (16%). Almost half are conducting DNA-related research. However, the average operating income for AAM firms was negative.

- Sixteen percent of respondents (160 firms) indicated "other" biotechnology applications as their business focus. Many of these companies reported that they develop and market tools to support biotech R&D such as synthetic DNA and protein products,

polymers for biochemical analysis and separations, biosensors, or computer hardware and software.

- The defense sector is one customer for a number of companies that have biotechnology-related activities, and national defense agencies are increasingly interested in biotechnology's capabilities. About 10% of survey respondents (105 firms) reported having held a defense-related contract in the past five years. They generally were larger firms with relatively higher levels of employment and net sales.

- Primary areas of activity for firms holding defense contracts included human health applications, animal health, and production of specialty chemicals and agriculture-based materials.

- R&D intensity (calculated as a ratio of R&D expenditures to net sales) was highest for the 41 firms that engage in environmental remediation and natural resource recovery. Research areas were highly concentrated, with 48% of companies conducting research in the areas of bioremediation and biofiltration and 45% citing gene probes and DNA markers.

Economic Performance

- The value added for respondents' businesses was at least $272.8 billion or 2.7% of U.S. gross domestic product (GDP) in 2001. Value added for biotech business lines was at least $33.5 billion or 0.33% of the $10 trillion U.S. GDP in that year.

- Biotechnology business lines demonstrated higher rates of growth, and capital and R&D intensity than did respondents' overall businesses. For example, in 2001 and 2002 growth for biotechnology net sales averaged just over 10%, while total net sales rose at an average annual rate of about 6%.

- In the recessionary year of 2001, growth in operating income of biotech business lines was slightly positive (1.1%) compared with a 3.9% decline for respondents' overall businesses. In 2002, operating income for the biotech business segment of firms expanded at twice the rate of growth for the entire businesses—14.1% versus 7%, respectively.

- During 2001, firms were investing about twice as much in their biotechnology-related lines of business as in their businesses as a whole. For example, capital expenditures represented 12.4% of total net sales for the biotech business lines, compared with 5.2% for all operations.

- Fifty-six percent of respondents reported either no operating income or negative operating income in 2001. Smaller firms reported a greater reliance for their biotech R&D on venture capital, angel investors, and IPOs. For example, about 44% of firms with 50 or fewer employees identified these sources of funding in 2001, compared with 2% of firms with more than 500 employees.

R&D Expenditures

- Biotechnology-related R&D expenditures amounted to $16.4 billion in 2001, about 10% of all U.S. industry R&D in that year. R&D intensity for biotech business lines was 33.4% in 2001, compared with 9.5% for firms' entire businesses and 4.3% for total U.S. corporate R&D spending. Also distinct from most other U.S. R&D companies, respondents generally spent more on research than on later stage development.

- Firms with 500 or fewer employees obtained their R&D financing in 2001 from different sources than did larger firms. These smaller respondents were much more likely to depend on venture capital, angel investors, and IPOs, while larger firms relied more on in-house resources or parent firm funding.

Workforce

- The population of companies engaged in biotechnology is dynamic and growth in the biotechnology-related workforce has been vigorous, averaging 12.3% annually for those companies that provided data for 2000–2002. Companies with 50 to 499 employees experienced the fastest growth, with an annual increase of 17.3%, while growth among larger responding firms was 6.2%. These figures compare to essentially no growth in U.S. non-farm payroll employment during this period.

- Firms reported that more than 66,000 employees could be classified as biotech-related technical workers. Scientists accounted for 55% of this total. Other occupations included science and clinical laboratory technicians (30%), engineers (8%), and R&D-focused computer specialists (6%). Companies also identified a number of employees with biotech-related responsibilities in administration and production, including supervisors, managers, and legal workers.

- The fastest growing biotech-related technical occupation was R&D-focused computer specialists, a category that grew at an annual rate of 21.8% during 2000–2002, adding 1,236 workers. However, more scientists were hired during the period (5,939), followed by science and clinical laboratory technicians (4,337).

- Smaller companies (those with fewer than 50 employees) reported difficulty in filling positions. Nearly half of these firms reported that more than 20% of their biotech-related positions had been unfilled for more than three months. This was true for only 1% of firms with more than 50 employees.

- Companies indicated that they rely heavily on U.S. workers, and specifically on local labor markets. Fewer than 6% of firms reported obtaining technical workers through foreign outsourcing. The largest concentration of such workers was reported to be R&D-focused computer specialists, who accounted for 28.8% of workers under contract abroad (12.4% of those under domestic contracts), but only 6.3% of the in-house technical workforce. This is consistent with the national trend of information technology occupations leading the offshore sourcing of professional-level technical workers.

- Half of all survey respondents are contemplating outsourcing some jobs domestically to U.S. firms. Only about 26% are thinking of outsourcing to foreign firms or facilities. More than 75% of companies stated that outsourcing to domestic firms provides 10% or less of their workforce, and 83% made the same statement with respect to foreign outsourcing.

Barriers to Business Competitiveness

- More than half of all respondents identified impediments to their firm's advancement of biotechnology research or product commercialization: regulatory approval process and costs (59%), and research costs and access to start-up capital (53% each).

- In addition to these three barriers, firms working in the area of AAM biotechnology were equally concerned about unfair foreign laws and public acceptance/ethical considerations. Companies engaged in environmental remediation and natural resource recovery applications also cited antiquated rules and regulations and unfair U.S. laws.

Competitive Strategies and Outlook

- Firms' near-term business strategies are focused primarily on developing technologies that can be licensed to others (the choice of 53% of respondents), acquiring technologies from other companies through licensing arrangements (47%) or joint venture arrangements (23%). Many companies also noted plans to refocus R&D activities or product development.

- Companies engaged in biotechnology research, development, and application generally are optimistic, with 75% indicating that they expect competitive prospects for their business operations over the next two years to improve "greatly" or "somewhat."

Only 46 firms (4.5%) believe their future competitive business prospects will decline "somewhat" or "greatly" over the same period. These are generally smaller firms with fewer than 100 employees and either no or negative operating income.

- Companies working in AAM applications were the most pessimistic, with nine companies (7.3%) indicating that business prospects were likely to worsen in the near future. Firms engaged in environmental remediation and natural resource recovery were particularly optimistic (no firm provided a negative response).

Chapter 1
Objectives and Methodology

Background

The idea for a comprehensive survey of the use and development of biotechnology originated in discussions between staff at the United States Department of Commerce (DOC), U.S. firms, biotechnology-related organizations, and other federal and state policymakers. These discussions underscored two facts: (1) the need for a more accurate understanding of the application and development of biotechnology in U.S. industries and the contribution of biotechnology to U.S. economic output, productivity growth, and national security and (2) the importance of developing more comprehensive objective measures and statistics about biotechnology in order to better support U.S. industries' innovation and competitiveness.

To assist policymakers and U.S. statistical agencies in developing "official" measures and statistics and to provide a useful benchmark about the current use of biotechnology in U.S. industry, DOC's Bureau of Industry and Security, Office of Strategic Industries and Economic Security (SIES)[1] and DOC's Technology Administration, Office of Technology Policy (OTP)[2] developed the survey instrument, *Critical Technology Assessment of Biotechnology in U.S. Industry (CTA* or *Critical Technology Assessment)* in 2002. A copy of the survey questionnaire is included in Appendix A.

The *CTA* survey collected information about companies' biotechnology activities, including their scientific capabilities, defense contracting, financial operations, investment, research and development (R&D) expenditures, employment, interaction with federal agencies, impediments to business growth, and business and market projections.

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[1] Within the Department of Commerce, SIES is the focal point for issues relating to the health and competitiveness of the U.S. defense industrial base. SIES works to maintain and enhance national and economic security by conducting primary research and analysis on critical technologies and defense-related industrial sectors. Congressional mandates and executive orders grant SIES the unique authority to conduct surveys and assessments of defense-related industries and technologies, and to monitor economic and trade issues critical to the U.S. industrial base. SIES's capabilities are leveraged through partnerships with a wide range of defense and civilian federal agencies, industry associations, state and local governments, and universities.

[2] The mission of the Office of Technology Policy (OTP) is to develop and advocate national policies to maximize technology's contributions to U.S. economic growth and competitiveness. OTP works with industry, the scientific community, and other government agencies to boost the development and adoption of new technologies through outreach, advocacy, and analyses. OTP is actively engaged in policy issues related to other emerging technologies such as nanotechnology, and such areas as technology transfer, development of a strong science and technology workforce, and technology-led economic development.

Objectives

This analytical report is intended to assist government policymakers and business officials in developing initiatives to improve the overall competitiveness of U.S. firms that develop and use biotechnology, and to enhance the capabilities of such firms that support national defense missions. It is also intended to provide information to federal agencies with missions that include managing surveys and data collection related to U.S. industries and their R&D activities. In addition, biotechnology firms may use this report to compare their characteristics with those reported by respondents. Educational institutions and scientific and economic development professionals may also find the report useful.

The three principal objectives of this assessment were as follows:

- To develop estimates of the economic scope and size of biotechnology activities in U.S. industries relative to the national economy;
- To estimate the economic performance, growth, trade, and markets; research and development expenditures; employment; interactions with the federal government; and defense orientation of firms that are developing and applying biotechnology; and
- To identify firms' perceptions of barriers to the development and use of biotechnology by U.S. industry.

Survey data were collected and analyzed to assess the characteristics and economic strength of U.S. companies engaged in biotechnology research or production of biotechnology products or research tools, or that use biotechnology processes in their manufacturing.

This analysis includes estimated contributions of biotechnology activity to the U.S. economy based on survey responses received.[3] These contributions include job generation, sales revenues, capital investment, exports, and support for R&D. Summaries of qualitative survey data—such as responding firms' perceptions of impediments to growth and future plans—also are presented.[4] This report does not provide estimates of biotech's nonfinancial contributions to U.S. society, such as increased lifespan and productivity from human health improvements; increased agricultural productivity; or cleaner, lower-cost manufacturing processes.

SIES and OTP developed the *Critical Technology Assessment* in consultation with DOC's International Trade Administration and Bureau of the Census; the National Institutes of Health; the National Institute of Standards and Technology; and the Departments of Agriculture, Energy, the Army, and the Navy. The survey was then field-tested with more than a dozen firms. The Biotechnology Industry Organization (BIO) and the State of Maryland, Montgomery

[3] For additional notes on methodology, see Appendix B.

[4] Additional data tables are provided in Appendix C.

County Department of Economic Development, assisted in this effort and also reviewed the final survey before it was sent to the Office of Management and Budget (OMB) for review and approval for compliance with the Paperwork Reduction Act.

The *CTA* was conducted in accordance with SIES's survey authority under the Defense Production Act of 1950, as amended (50 U.S.C. App. Sec. 2155). SIES is delegated survey authority under Section 705 and Executive Order 12656 to collect basic economic and industrial information from industry. All individual firm data remain confidential and are protected by law.

Definition of Biotechnology

For the purposes of this assessment, the interagency study team defined biotechnology as the application of molecular and cellular processes to solve problems, conduct research, and create goods and services. Under this definition, biotechnology includes a diverse collection of technologies that manipulate cellular, subcellular, or molecular components in living things to make products, discover new knowledge about the molecular and genetic basis of life, or modify plants, animals, and microorganisms to carry desired traits.[5] Further, the survey specified that biotechnology pertains to molecular, cellular, and genetic processes applied to develop products and services for commercial purposes. The hallmark of biotechnology is cellular and genetic techniques that manipulate cellular and subcellular building blocks for applications in various scientific fields and industries such as medicine, animal health, agriculture, marine life, and environmental management.

Scope of Assessment and Survey Population

In the United States, biotechnology is developed and applied by publicly traded and proprietary companies, university-based institutions, government agencies, and nonprofit enterprises. This study incorporates data obtained from public and privately traded companies and nonprofit enterprises operating domestically that identified themselves as biotech firms or organizations. The survey was mailed to both U.S.- and foreign-owned businesses existing within the United States. Excluded from this study are government organizations, universities, and foreign businesses operating abroad.

Several sources were used to identify companies for inclusion in the initial survey mailing list. These sources included membership lists provided by trade organizations such as BIO, corporate biotechnology directories, and larger statistical databases, such as the OneSource Information

[5] Such technologies include, but are not limited to recombinant DNA methods, cloning, DNA sequencing, polymerase chain reaction (PCR) amplification, oligonucleotide and protein synthesis, gene and protein markers, microarrays, RNA interference, monoclonal antibodies, transgenic organisms, bioinformatics, and biosensors. See Appendix D.

Services "CorpTech" database, which includes publicly traded firms from all industrial sectors. In addition, several state and federal agencies provided suggestions.

In general, the initial survey population of 3,189 U.S. companies was drawn from firms included in one of these three databases and that appeared to meet the survey definition of biotechnology, as determined by a description of their activities and/or their names. Surveys were mailed to companies in August 2002. Responses were received from 61% (1,945) of companies surveyed. Of these, 1,031 firms (53% of all respondents) confirmed that they were performing biotechnology activities relevant to this assessment and provided sufficient data for analysis.[6]

This analysis is based on survey responses from companies that engage in biotechnology research, create biotechnology products or research tools, and/or use biotechnology processes in their manufacturing—either as one of several business lines or as their sole business. Respondents whose business activities appeared to differ from the survey's definition of biotechnology were not included in the final analysis.[7]

Methodology

The *CTA* survey was modeled, in large part, upon survey efforts that have been undertaken by other national governments and discussions that have been held in the statistical group of the Organization for Economic Cooperation and Development (OECD).[8] To date, Canada has the most experience in developing and administering national biotechnology surveys, having completed four surveys since 1996.[9] In an effort to increase international comparability among survey results and to try to adopt the best practices developed by others, portions of the *CTA* survey terminology and structure were modeled after Canadian biotechnology surveys and other national surveys completed prior to 2002.[10]

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[6] See Appendix B, Methodology, for a discussion of the survey population and its treatment in calculating share-weighted growth rates and other quantitative measures.

[7] Examples of companies exempted from this study are firms that provide business consulting services to scientific companies; biotechnology brokers that purchase licenses for biotechnology products and sell those licenses to other biotechnology companies; firms that supply contract personnel to biotechnology companies or that contract services such as clinical trials; research firms that engage in related but non-biotechnology sciences such as biochemistry and biology; and firms that solely use biotechnology applications that are over 20 years old, such as traditional animal/plant breeding techniques and the use of yeast in making bread, beer, wine, and cheese.

[8] The Organization for Economic Cooperation and Development (OECD includes a statistical group, the Working Party of National Experts in Science and Technology Indicators (NESTI). NESTI's subcommittee on biotechnology has met five times (most recently in May 2003) to discuss appropriate survey methodologies for assessing certain aspects of national biotechnology development and adoption.

[9] The 2003 survey is in progress. Results of the 2001 Canadian biotechnology survey may be found at http://www.statcan.ca/english/IPS/Data/88F0006XIE2003005.htm (viewed August 8, 2003).

[10] For example, the categories of biotechnology applications and the more specific technologies listed in *CTA* question 5 resemble industry distinctions made in the most recent Canadian biotech survey.

Nevertheless, data collected from the *CTA* and presented in this report will differ from, and may not be comparable to, survey results reported by other studies of biotechnology firms. Such variation usually occurs because methodological differences in survey design and interpretation result in different data and conclusions. The following information and Appendix B are intended to clarify the methodological underpinnings of the data presented in this report.

As noted above, the survey questionnaire for the *Critical Technology Assessment* was sent to companies that were drawn from public listings of biotechnology companies, rather than being sent to a random sample of all companies in a particular industry sector, such as agriculture or chemicals. This approach was used because the objective of the study was to ask questions of companies currently engaged in the use and development of biotechnology, rather than extrapolating information to the national level based on a projectable scientific sample of firms. However, it should be recognized that the results presented here do not represent all U.S. firms engaged in biotechnology, and therefore are not national estimates. There are undoubtedly firms that were not included in the sources used to compile the mailing list for the *CTA*; as a result, total estimates of financial data presented here are likely to understate the use of biotechnology in U.S. industries.

Another example of how different survey results reflect differences in survey population can be seen in comparing the population of respondents to the *CTA* with those in private surveys of biotech activity, such as Ernst & Young's (E&Y) annual reports on the biotechnology industry. According to notes provided in the E&Y annual surveys, respondents include firms working in medical biotechnology, agricultural biotechnology, and environmental and industrial biotechnology, but exclude large pharmaceutical companies, contract research organizations, and equipment manufacturers. As noted above and in footnote 5, the respondent population for the *CTA* survey excludes services firms that conduct clinical trials and certain other services firms, but includes most large pharmaceutical companies and a number of companies that produce "tools" for biotechnology firms. Such differences in survey scope may result in different statistics. (For example, *CTA* survey respondents indicated a total of 130,305 biotech employees toward the end of 2002, while E&Y reported employment of 191,000 in 2000).[11]

Quantitative differences may also arise because of the way questions are asked. Some private statistical reports present employment figures based on head count, while many government-sponsored national surveys ask respondents to provide information about the number of full-time equivalent employees (FTEs).[12] Similarly, the *Critical Technology Assessment* asked companies to provide information about net sales; other surveys may ask for net revenues.[13]

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[11] www.bio.org/er/statistics.asp (viewed May 20, 2003).

[12] The *CTA*'s employment-related questions did not specify whether respondents should calculate full-time employee equivalents (FTEs) on the basis of calendar or fiscal years. Analysis assumes that employment responses for questions 12 and 13 are for calendar year 2002 through completion of the survey.

[13] See Appendix D for a glossary that includes financial terms.

Other Methodological Notes

Firms with 50 or fewer employees were not required to submit quantitative financial data for multiple years.[14] While lessening the burden for 59% of respondents, this limited the robustness of time series data. It should be noted that only those firms that provided data for the 2000–02 period were included in growth rate calculations (see Appendix B for more methodological detail). Single-year financial data are presented for 2001, which was a recessionary year for the national economy.[15] Employment figures are based on respondent employment for 2002, unless otherwise noted.

Recipients of the survey were asked to identify themselves as biotechnology companies and confirm that their company was engaged in biotech-related activities. In some cases, respondents who develop or produce biotechnology products initially claimed exemption. In other cases, respondents claimed to be biotechnology companies, but a closer examination of their manufacturing processes revealed that the advanced biotechnologies of principal concern in this survey were not actually used in production. Every effort was made to ensure that final survey data reflected the inclusion of appropriate companies.

Firms were not asked to segment their sales, employment, and related information, and could indicate multiple applications for their biotech activities;[16] in fact, 64 of the respondents elected more than one "primary" application area to describe their biotech activities.[17] Therefore, financial and employment data that are presented by application in Chapter 3 should only be interpreted as data for all firms that selected that application as a "primary" or "secondary" focus of their biotech-related activities. Because many respondents indicated that they work in several fields of biotechnology, application-specific data cannot be summed to obtain estimates of total biotechnology-related employment, sales, capital expenditures, research and development expenditures, or other financial and quantitative data.

Survey responses are not establishment-specific; that is, some survey responses consolidated information from large firms' multiple business operations. This limits the degree to which conclusions can be drawn about the geographic distribution of biotech firms and their financial impact and number of employees by state. For example, if some respondents have operations in several states but reported aggregated employment information for all company

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[14] *CTA*, pages 8, 10, 12.

[15] According to the National Bureau of Economic Research (NBER), economic data indicate that 2001 was a recessionary year.

[16] *CTA*, pages vii–viii.

[17] All respondents were asked to indicate their "primary" and "secondary" areas of biotechnology activities in at least one of eight different areas. Although all respondents were classified into at least one category of specialization, some biotechnology activities can be used in several different areas of application, resulting in multiple application categories for a single respondent. For example, a laboratory might have indicated that it performs vaccine research in both human and animal health. In such a case, responses would be reported and analyzed in both application categories.

establishments, the total number of company employees would be attributed only to the single geographic location of the reporting entity.

Organization of the Report

The remainder of this report is organized as follows. Chapter 2 provides an overview of the use and development of biotechnology by U.S. industries, as reported by survey respondents. It also includes some comparative information based on size of companies and their involvement in specific areas of biotechnology-related activity.

Chapter 3 continues this focus by presenting disaggregated information about firms' research focus, sources of funding for biotechnology-related research, and primary export markets, based on responses of firms that indicated a focus in one of seven "application" categories. It also provides information about respondents that have held defense-related contracts. The seven application categories of Chapter 3 are human health; animal health; agriculture and aquaculture; marine and terrestrial microbial applications; industrial and agricultural processing; environmental remediation and natural resource recovery;[18] and "other."[19]

Chapter 4 presents analysis of aggregated company responses related to the financial performance and economic contributions of firms' biotechnology-related business lines and their entire business. Chapter 5 discusses respondents' R&D activities. In these chapters, some data that are reported for biotechnology firms are compared with other firms in a particular sector or other information is provided to offer context for the reported responses.

Chapter 6 analyzes responding firms' employment and workforce characteristics. Finally, Chapter 7 discusses the leading competitive factors identified by respondents as affecting their advancement of biotechnology research or product commercialization, including regulatory requirements, access to capital, and patenting practices. The chapter also summarizes the competitive strategies of survey respondents and their future outlook.

[18] To preserve confidentiality of data, analysis of two application areas—environmental remediation and natural resource recovery—is aggregated for purposes of this report, due to the small number of responses.

[19] Companies describing themselves as "other" engage in activities outside the seven major application areas defined by the survey instrument. For example, such companies manufacture biotechnology research tools such as hardware and software, biosensors, synthetic DNA and protein products, biochemical polymers, and other tools to assist researchers working in multiple biotechnology applications.

Chapter 2
Overview

New technologies can transform industry by creating new products, improving production processes, and accelerating the pace of innovation. Biotechnology is one example of a set of emerging technologies that have the potential to contribute to economic growth. Although the manipulation of biological architecture is both ancient (fermentation and brewing) and current (splicing genes and using computers to analyze nucleotide sequences and protein structures in ways that help to pinpoint drug targets), the full economic and social impacts of new developments in biotechnology have yet to be realized.

Patent data underscore the dynamic and rapidly evolving nature of biotechnology. In the last quarter of 2002, respondents indicated that they had pending U.S. patent applications for 32,304 new biotech-related products or processes, compared to 23,380 current U.S. biotechnology-related patents in their portfolios.[20] Other survey data[21] underscore the point that recent discovery, development, and application of biotechnologies are not only creating entirely new types of products and services, but that biotech processes and products are now applied in all types of manufacturing, agriculture, aquaculture, and even at the microbial and nano-scales.

This chapter describes reported establishment dates of the 1,031 survey respondents and their geographic distribution, as well as characteristics of these companies by firm size. It also provides insight about the types of industries that have companies pursuing the development and use of biotechnology in the United States today.

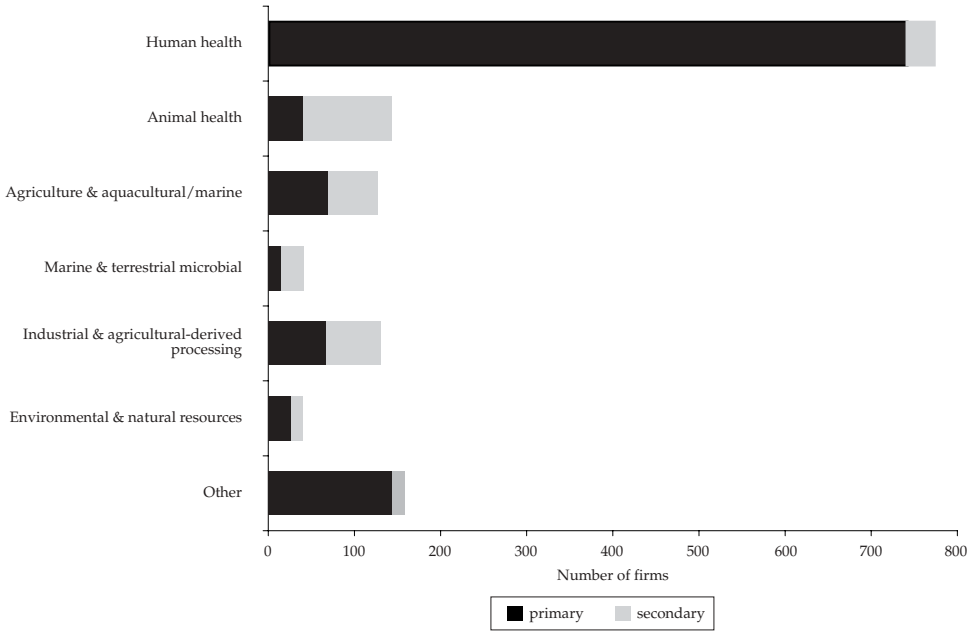
Variety of Applications

Five of 45 survey questions asked respondents to identify their companies' biotechnology-related activities. In addition to qualitative responses, respondents indicated "primary" and "secondary" areas of biotech activity in one or more of eight categories: human health; animal health; agricultural and aquaculture/marine; marine and terrestrial microbial; industrial and agriculture-derived processing; environmental remediation; natural resource recovery; and "other." More than 76% of all respondents (780) selected "human health" as their primary or secondary application focus, while 12% to 14% of respondents chose one of three other categories—"animal health," "agriculture and aquaculture," or "industrial and agriculture-derived processing"—and 4% to 5% chose either "marine and terrestrial microbial" or "environmental remediation and natural resource recovery" (Figure 2.1). Sixteen percent of respondents (160) indicated "other" biotechnology applications as their business focus. Many of these companies reported that they develop and market tools to support biotech R&D such as synthetic DNA

[20] *CTA*, question 34, page 13.

[21] *CTA*, question 5, page 2.

Figure 2.1: Primary and Secondary Activities by Biotech Application



Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Technology in U.S. Industry,* p. vii, August 2002.

and protein products, polymers for biochemical analysis and separations, biosensors, or computer hardware and software.

Statistical Classification of Biotechnology Companies

Firms involved in biotechnology are not separately classified as a single industry for purposes of U.S. Department of Census surveys of research, manufacturing, or service firms. Nor are they classified as a distinct industry within either the North American Industry Classification System (NAICS) or its predecessor, the federal Standard Industrial Classification (SIC).

There are several reasons for this. One is that the application and development of "modern" biotechnologies is relatively recent, and incorporation into national statistical accounts requires a specific process[22] and takes some time. More important, as biotechnology is applied to a widening array of industrial applications, developing a single classification category for firms engaged in biotechnology-related activity is proving to be complex and difficult.

To gain a better understanding about the breadth of industries engaged in biotechnology, survey respondents were asked to provide their NAICS code or SIC code. Respondents identified more

[22] See http://www.census.gov/epcd/naics07/index.html#part3, viewed August 12, 2003.

than 60 four-digit NAICS categories. These responses indicate that firms in industries as diverse as "paints, coatings and adhesives" (3255), "semiconductor and related device manufacture" (3344), and "waste management and remediation services" (5629) are engaged in biotechnology-related activities. Despite this diversity, however, almost 65% of survey respondents were classified in either one of two broad categories (Table 2.1): "medical substances and devices" (NAICS category 3254) or "scientific R&D services" (NAICS 5417).

NAICS-based analysis is particularly useful in understanding the statistical requirements and possibilities for measuring biotechnology-related economic activity going forward. Because biotechnology activities are embedded in many industries, creating new separate statistical categories would require adjusting historical industry groupings. Understanding the magnitude of potential adjustments is one piece of important information for statistical agencies as they grapple with how best to measure the development, application, and sales of biotechnologies in the U.S. economy. Survey data should be useful in crafting subsequent survey efforts directed at U.S. companies engaged in biotechnology.[23]

The North American Industry Classification System (NAICS)

The North American Industry Classification System (NAICS) has replaced the U.S. Standard Industrial Classification (SIC) system. Developed in cooperation with Canada and Mexico, NAICS represents one of the most profound changes for statistical programs focusing on emerging economic activities. NAICS, developed using a production-oriented conceptual framework, groups establishments into industries based on the activity in which they are primarily engaged. Establishments using similar raw material inputs, similar capital equipment, and similar labor are classified in the same industry. The structure of NAICS is hierarchical. NAICS classifies all economic activities into 20 industry sectors. Five sectors are mainly goods-producing sectors and 15 are entirely services-producing sectors. NAICS uses a six-digit coding system to identify particular industries and their placement in this hierarchical structure of the classification system. The first two digits of the code designate the sector, the third designates the subsector, the fourth designates the industry group, the fifth designates the NAICS industry, and the sixth digit designates the national industry. This six-digit hierarchical structure allows greater coding flexibility than the four-digit structure of the SIC. NAICS allows for the identification of 1,170 industries, compared to the 1,004 found in the SIC system.

Establishment Dates and Geographic Distribution

Of the 994 survey respondents that reported establishment dates, about 14% (135) were established prior to 1980; the oldest was established in 1802. Seventy-three percent (728) have been established since 1986, with 29% emerging during 1993–2001. It appears that the rate of growth in the number of companies engaged in biotechnology in the United States has trended upward, although with some irregularity, during the past decade, if survey data are indicative of national trends (Figure 2.2).

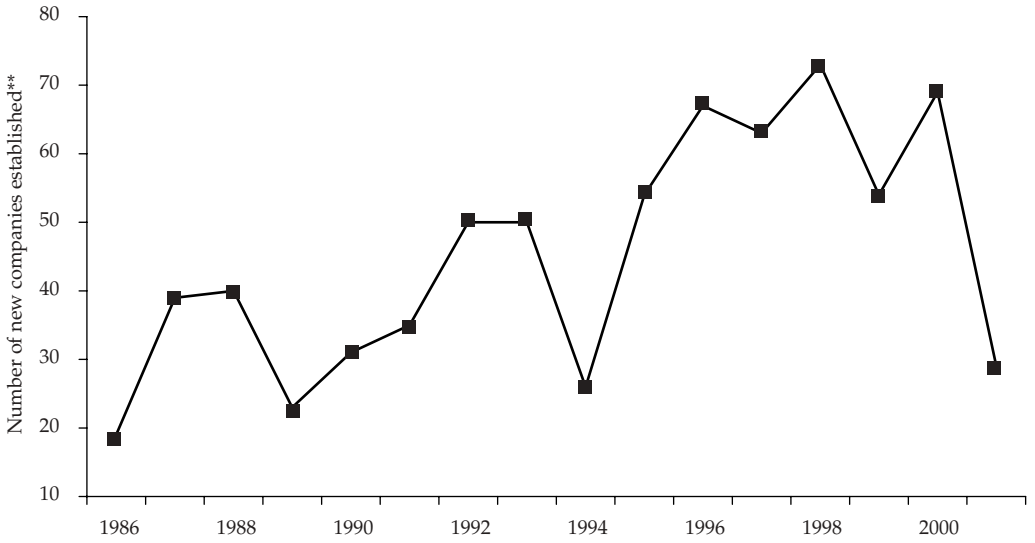
[23] For example, biotechnology-related questions might be included on national R&D surveys or certain industry surveys directed at companies in these NAICS categories. Currently, the National Science Foundation includes biotech-related questions on its their annual R&D survey sent to a random sample of U.S. firms. The U.S. Bureau of the Census also includes biotechnology-related questions on its R&D services surveys.

Table 2.1: NAICS Codes Reported by *CTA* Respondents

Industry	NAICS codes	Number of companies per industry	Percent share of companies
Basic industries & materials			
Agriculture, forestry, fishing & hunting	11	11	1.1
Food, beverage, tobacco manufacture	311,312	16	1.6
Furniture & laboratory apparatus manufacture	337,339111	7	0.7
Other basic industries activity	22,23,323,327,3399	5	0.5
Plastics & rubber products manufacture	326	3	0.3
Paper & wood manufacture	322	1	0.1
Chemical manufacture			
Basic chemical manufacture	3251	19	1.8
All other chemical product manufacture	3250,3259	15	1.5
Agricultural chemical manufacture	3253	8	0.8
Resin, synthetic rubber & fibers manufacture	3252	2	0.2
Paint, coatings, adhesives, cleaning, surface agent	3255,3256	1	0.1
Information & electronics			
Instrument manufacture	334511-19	34	3.3
Software publishers	5112	5	0.5
Computer systems design & related services	5415	2	0.2
Motion picture & sound recording industries	512	1	0.1
Semiconductor & related device manufacture	334413	1	0.1
Computer peripheral equipment & terminal manufacture	334113,334119	1	0.1
Machinery manufacture			
Commercial & service industry machinery manufacture	3333	1	0.1
Other industrial machinery manufacture	33321,33322,333291-4, 333298,3334,3335,3339	5	0.5
Medical substances & devices			
Non-diagnostic biological product manufacture	325414	127	12.3
Pharmaceutical & medicine manufacture	3254* & 325412	117	11.3
In-vitro diagnostic substance manufacture	325413	50	4.8
Medicinal & botanical manufacture	325411	7	0.7
Medical instruments, equip. & supplies manufacture	334510	36	3.5
Various services			
Scientific R&D services	5417	333	32.3
Profes., sci., & tech. services excpt test lab. computer & sci. R&D serv.	54 excpt 54138,5415 & 5417	23	2.2
Testing laboratories	54138	20	1.9
Medical & diagnostic laboratories	6215	20	1.9
Wholesale & retail, transport & warehousing	42,44,45 excpt 45411,48,49	15	1.5
Management of companies & enterprises	55	6	0.6
Other services	61,62,71,72,81 excpt 6215	4	0.4
Admin., support, waste management & remediation	56	1	0.1
No industry identified	**NA**	**134**	**13.0**
TOTAL		**1,031**	**100.0**

*Twenty-six of 301 medical substances firms are classified under the more general NAICS code 3254, pharmaceutical & medicine manufacture, which means they produce a range of products that if exclusively produced could othewise be designated under one of the more detailed (six digit) codes of this sector. These companies are included with the firms classified under code 325412, pharmaceutical preparation manufacture.

Figure 2.2: Respondents' Establishment Dates, 1985–2001*



*2002 data are excluded due to difficulty identifying all new firms to receive the survey and because the survey was conducted before the end of 2002. To a lesser extent, 2001 data may somewhat undercount the complete number of firms established in that year.

**Based on responses from 722 firms, representing 73.1% of the 959 respondents that provided establishment data.

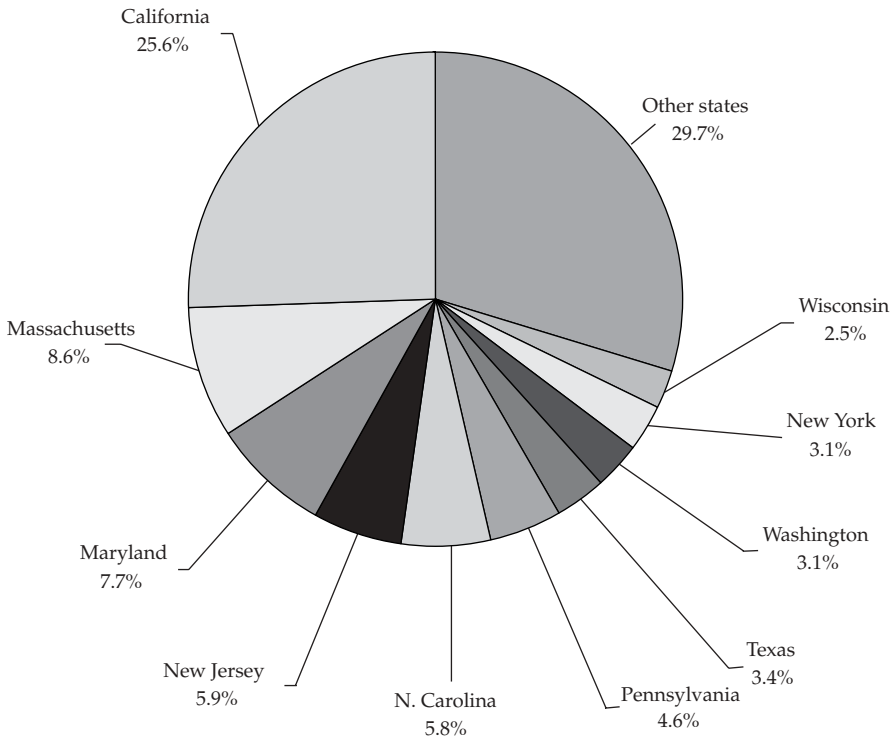
Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Technology in U.S. Industry,* question 1, p. 1, August 2002.

Since biotech-related activity is being pursued in a wide variety of industries in the United States, it is not surprising that virtually every state has at least one biotech company. Survey respondents are headquartered in 46 states, but 70% reside in just 10 states.[24] Leading all states, California companies accounted for 26% of all respondents—an amount approaching the 30% of all respondents located outside the "top ten" states (Figure 2.3).

During the 1997–2001 period, California expanded its share of newly established biotech firms, accounting for 38% of responding companies that were established during this period. North Carolina, Maryland, and Massachusetts followed California with 11%, 9%, and 6% of new biotech establishments, respectively (Figure 2.5).

[24] As noted in Chapter 1, survey responses are not establishment-specific; that is, some survey responses consolidated information from large firms' multiple business operations. This limits the degree to which conclusions can be drawn about the geographic distribution of biotech firms and their financial impact and number of employees by state.

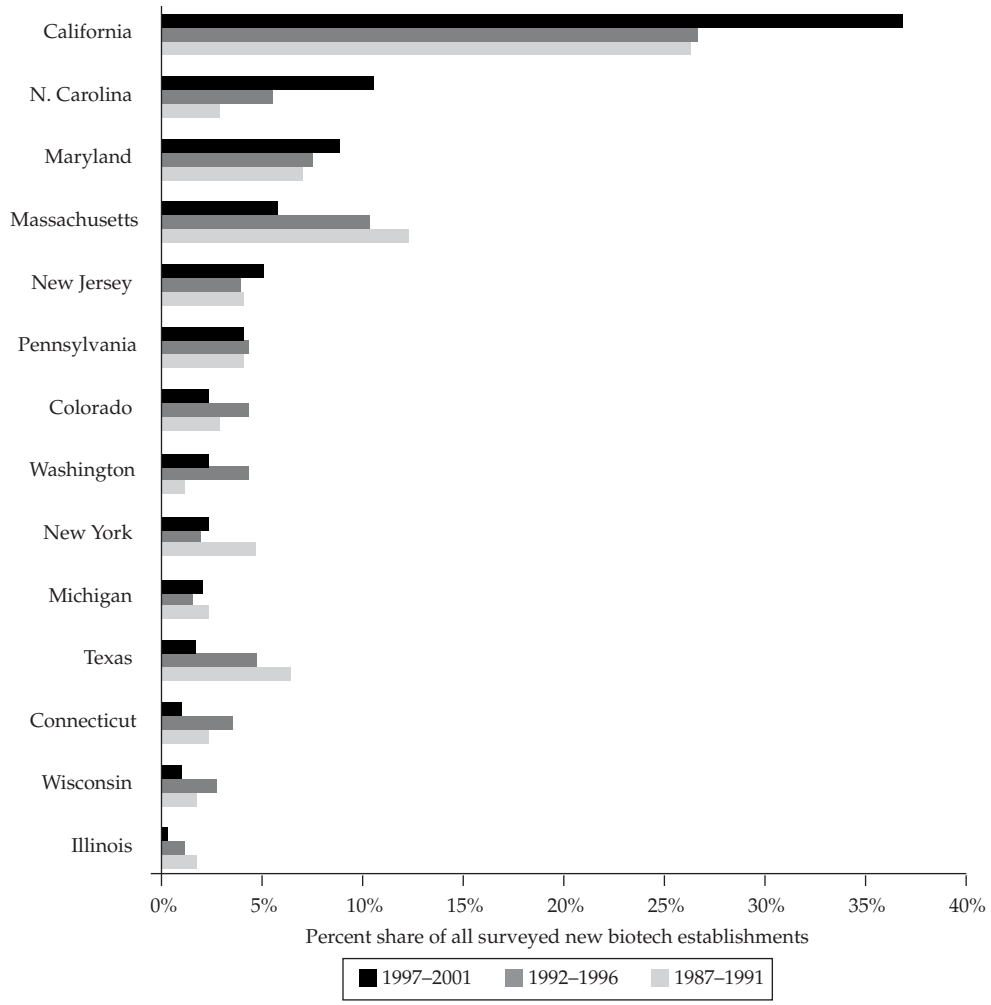
Figure 2.3: Top Ten Biotech States by Number of Firms, 2001



The top ten states account for 725 biotech companies or 70.3% of all the survey respondents.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Technology in U.S. Industry,* question 1, p. 1, August 2002.

Figure 2.4: State Share of New U.S. Biotechnology Companies,* 1987–2001

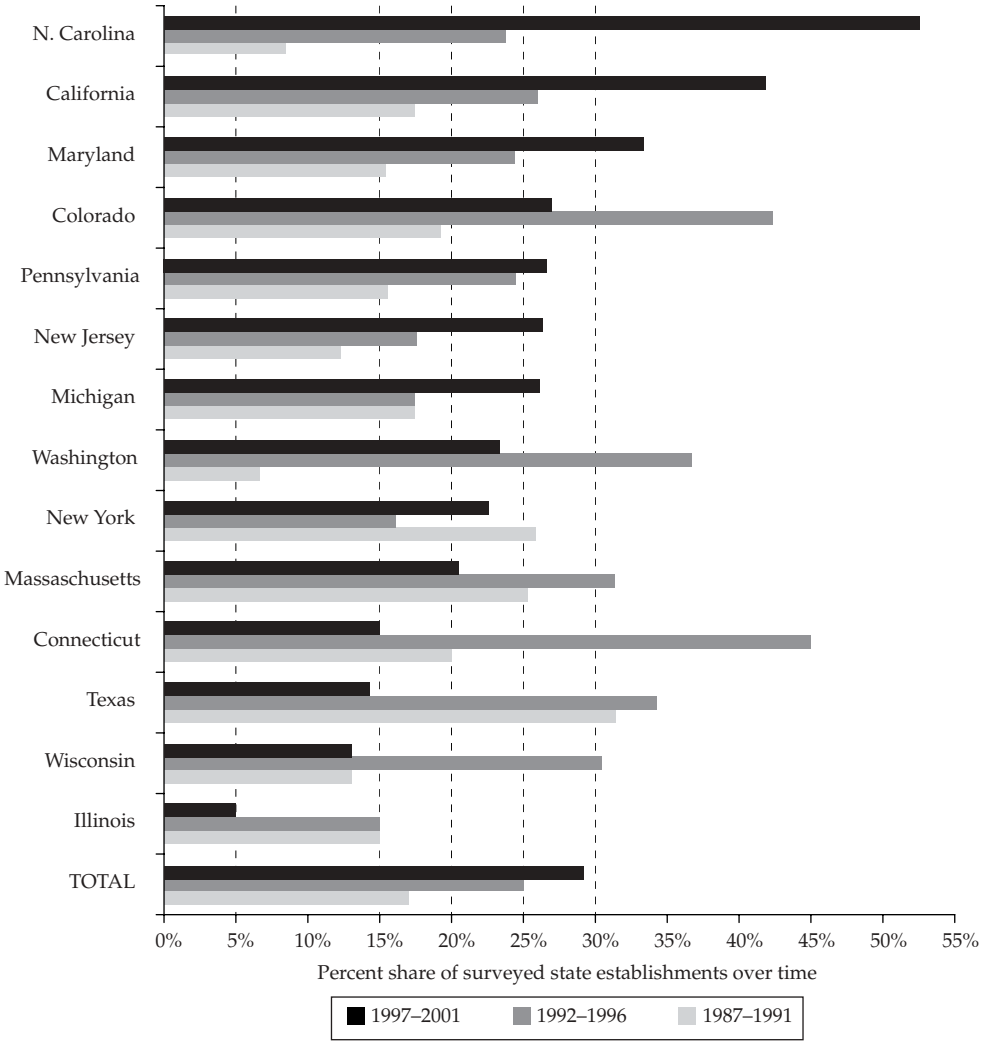


*Nine-six and four-tenths percent of responding firms reported establishment dates. Data include states with 20 or more firms that answered survey question 1, p. 1.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Technology in U.S. Industry,* question 1, p. 1, August 2002.

However, additional insight is gained by examining growth (on a percentage basis) in the relative number of new biotechnology companies established within individual states. As shown in Figure 2.5, North Carolina was the front-runner in adding new biotech companies during the most recent period. The state increased its total number of firms by 52.5% during 1997–2001, up from 23.7% during the previous period.

Figure 2.5: Growth in New Biotechnology Establishments by State*, 1987–2001



*Nine-six and four-tenths percent of responding firms reported establishment dates. Data include states with 20 or more firms that answered survey question 1, p. 1.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Technology in U.S. Industry,* question 1, p. 1, August 2002.

Ownership

Of companies that provided details about their ownership, 87% indicated that they were solely owned by U.S. interests at the end of 2002.[25] European nations account for the vast majority of foreign-owned companies, with the United Kingdom, Germany, and France leading all other countries except Japan (Table 2.2). About 3% of all respondents reported that they were entirely owned by foreign concerns in one of these four countries.

Table 2.2: Distribution of Foreign Ownership among Companies Reporting Foreign Ownership, 2001 (in percentages)*

United Kingdom	19.0
Germany	17.0
France	15.0
Japan	15.0
Sweden	8.0
Canada	7.0
Switzerland	5.0
Australia	3.5
Denmark	3.5
Belgium	2.0
Hong Kong	1.4
Hungary	1.4
Italy	1.4
Luxembourg	1.4
Netherlands	1.4
Ireland	1.4

*Includes firms reporting 80%–100% foreign ownership. Totals do not add up to 100% due to rounding.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Financial Perspective

Based on responses to the *Critical Technology Assessment* survey, it appears that the magnitude of U.S.-based businesses that are working in biotechnology research, development, and applications is substantial. When describing their entire business operations, survey respondents reported more than 1.1 million full-time equivalent employees (FTEs) and had overall 2001 annual net sales around $567 billion, operating income of $100.5 billion, capital expenditures of $29.5 billion, and R&D expenditures of $41.6 billion. Although on an aggregate basis companies' biotechnology-related undertakings appear to be only a fraction of their overall business activities (Table 2.3), accounting for 9% of net sales, 9% of operating income, and 21% of capital investment, R&D expenditures for biotech business lines accounted for almost 40% of total reported R&D expenditures. Moreover, for 90% of survey respondents, biotechnology-related activities constituted over 75% of their net sales, employment, or capital expenditures. These companies generally are smaller firms with fewer than 500 employees.

Table 2.3: Financial Data for Respondents: Total and for Biotech Business Lines, 2001

	Total ($000)	Biotech ($000)	Biotech/Total (%)
Net Sales	566,985,000	50,472,720	8.9
Operating Income	100,516,300	9,367,822	9.3
Capital Expenditures	29,535,620	6,244,325	21.1
R&D Expenditures	41,590,290	16,440,990	39.5

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

[25] *CTA,* question 2, page 1. Note that most surveys were returned by November 2002, so actual ownership on December 31, 2002, may differ slightly.

It is important to note that the preponderance of respondents that are focused on human health applications can obscure important distinctions between firms engaged in other types of biotechnology applications. Respondents whose businesses focus on human health applications accounted for 90% of all reported biotech employment, 93% of reported biotech net sales, 98% of all biotech operating income, 94% of all biotech capital expenditures, and 95% of all reported biotech R&D expenditures. However, companies engaged in agriculture/aquaculture and environmental-related biotech applications have somewhat different business strategies and competitive concerns than do those engaged in human health. In order to provide information about other areas of focus for firms engaged in biotechnology, Chapter 3 discusses company responses aggregated by application category.

Business Characteristics by Firm Size Category

Firms engaged in biotechnology activities vary greatly in size and scope. At one end of the spectrum, there are small dedicated biotechnology companies that focus only on research and that operate primarily on venture capital, grants, initial public offerings (IPOs), and collaborative agreements. At the other end of the spectrum, there are a number of large, diversified firms with well-established production and distribution systems and greater in-house resources. These companies devote a portion of their research activities to biotechnology-related product development, produce biotechnology products, or use biotech processes in production.

From the perspective of firm size (based on number of total reported employees[26]), survey respondents range along this spectrum, although the number of small firms far exceeds the number of large companies. More than 92% of respondents (946) that reported their employment reported fewer than 1,000 employees, 90% (917) have 500 or fewer employees, and 59% (600) have 50 or fewer employees. Nineteen respondents had more than 15,000 employees (Figure 2.6).

Analysis of survey data revealed important distinctions across *all* types of biotech activities, based on firm size. For example, smaller companies (those with 500 or fewer employees) reported obtaining their 2001 biotech R&D revenue and financing from very different sources than did larger companies with 500 or more employees. Respondents with 500 or fewer employees are much more likely to depend on venture capital, angel investors, and initial public [stock] offerings (IPOs) to finance their biotechnology-related R&D activities than are larger companies. These mechanisms were even more important for firms with fewer than 50 employees (Table 2.4). About 48% of survey responses for firms of this size identified these types of financing mechanisms as funding sources in 2001.[27] In-house revenues and parent firm funding were indicated in about 54% of responses for this group.

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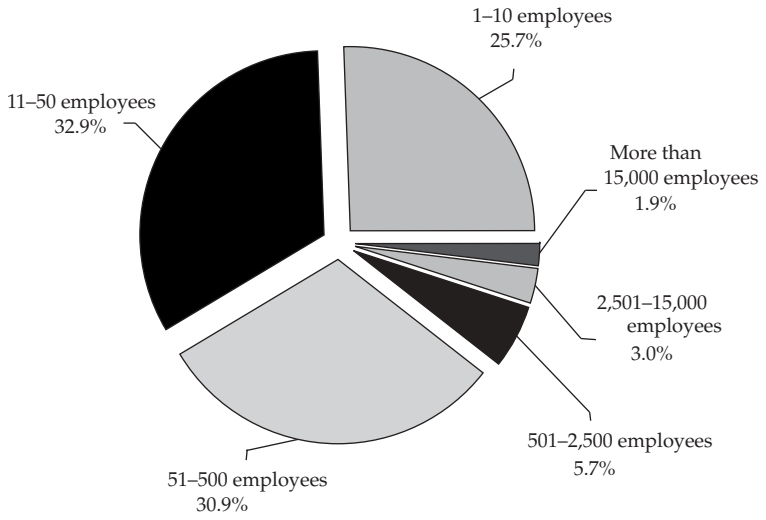
[26] Companies were asked to provide information about the number of full-time equivalent employees (FTEs) they employed. A total of 1,025 firms provided data on their 2001 employment. Throughout this report, the terms "employee" or "employees" are used interchangeably with FTE.

[27] *CTA*, question 29, page 11.

Figure 2.6: Distribution of Responding Firms by Firm Size Category



Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Technology in U.S. Industry,* question 12, p. 4, August 2002.

Table 2.4: Funding Sources by Firm Size, 2001

Firm Size	Number of Firms	In-House Revenue	Parent Firm Funding	Conventional Loans	Angel Investors	Venture Capital Firms	Initial Public Offering	U.S. Gov't Loan/ Grant	State Gov't Loan/ Grant	Foreign Gov't Loan/ Grant	Private Research Grants
No Response	3	1	1	0	0	1	0	0	0	0	0
0	5	2	2	0	0	0	0	0	0	0	0
1–10	217	114	10	11	53	29	2	61	5	1	9
11–50	308	143	20	14	66	97	5	71	13	1	13
51–500	296	174	30	17	13	65	33	65	8	5	15
501–2,500	51	44	7	1	0	1	1	8	2	1	3
2,501–15,000	30	26	6	0	0	0	0	2	2	0	1
>15,000	19	14	5	0	0	0	0	4	0	0	2
Total	929	518	81	43	132	193	41	211	30	8	43

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry*, August 2002.

Smaller respondents (those with 500 or fewer FTEs) also reported more frequently that federal and state loans and grants provided funding for their biotechnology R&D—19.2% of smaller firms in contrast to 11% of larger companies. This may be due in part to the criteria of some grant programs, such as the Small Business Innovation Research (SBIR) program,[28] which are available only to small and medium-sized businesses. Smaller companies also reported receiving more private research grants and grants from foreigners in 2001, although the dollar amounts were not disclosed.

In contrast, respondents that reported employment levels of 501 to 15,000 employees identified venture capital, angel investors, and IPOs as funding sources in 2001 in just 1% of all responses. In fact, only one company in this group indicated that venture capital provided funds in 2001. As might be expected, larger firms appear to self-finance their biotechnology-related R&D activities; 64.2% of responses pointed to in-house or parent firm funding.

The importance of export revenues also appears to vary depending on firm size. Even though 27.4% of the smallest firms (1–10 employees) indicated that they were exporting, exports accounted for only 6.1% of their total biotechnology sales. However, when all firms with 500 or fewer employees are examined, smaller firms account for about half of all biotech exports. Almost 57% of mid-sized firms (501–2,500 FTEs) indicated that they were exporting, and those firms reported exports sales of $2.67 billion, or 25.6% of total biotechnology export sales. Clearly, this group of firms is significantly engaged in the international market—more so than any other single group of firms, including even the largest firms (Table 2.5).

International markets account for at least 15.9% of net biotechnology-related sales for U.S.-based companies. In 2001, exports of biotech-related products and services accounted for at least $8 billion in revenues.[29] (See Chapter 7 for more information about respondents' exports.)

Analysis of data based on firm size also reveals that in addition to differences in sources of revenue for smaller and larger respondents, there are differences in the way companies engaged in biotechnology spend their revenues. For example, companies reporting 500 or fewer employees accounted for 13.5% of total reported biotechnology net sales but a disproportionately large share of total capital expenditures (26.7%) and R&D expenditures (34.4%), compared to their larger counterparts (Table 2.6).

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[28] Under the SBIR, 10 federal agencies reserve a portion of their R&D funds for annual awards to small businesses. Initial (Phase 1) awards may range up to $100,000. Eligibility criteria include the following: (a) firms must be American-owned and independently operated, (b) they must be for-profit, (c) the principal researcher must be employed by the firm, and (d) company size is limited to 500 employees. See http://www.sba.gov/SBIR/indexsbir-sttr.html for more information.

[29] Firms were asked to provide an estimate of how much exports contributed to their annual revenues (*CTA*, question 29, page 11). The survey also asked for firms' annual net sales (*CTA*, question 24, page 8). This estimate is based on net sales and assumes that revenues are greater than net sales.

Table 2.5: U.S. Biotech Exports by Firm Size, 2001

Firm Size	Total Firms Reporting	Total Firms Exporting Biotech	Exporting Firms (%)	Total Biotech Sales ($)	Total Biotech Export Sales ($)	Exports Share of Total Biotech Sales (%)
1–10	263	72	27.4	371,918	22,757	6. 1
11–50	337	104	30.9	515,067	95,892	18.6
51–500	317	120	37.8	5,928,568	1,009,687	17.0
501–2,500	58	33	56.9	10,457,482	2,673,974	25.6
2,501–15,000	31	14	44.9	15,464,259	2,374,795	15.4
> 15,000	19	9	47.4	17,733,423	1,855,163	10.5
Total	1,025	352	34.4	50,470,717	8,032,268	15.9

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Also, as noted in Table 2.7, smaller firms fared much better in terms of capital and R&D expenditures as a percentage of net sales, 24.4% and 83.1%, respectively, than did their larger counterparts (10.5% and 24.7%, respectively). R&D intensity of these smaller firms (measured as R&D expenditures per FTE) was also higher than the larger firms'. However, capital intensity (measured as capital expenditures per FTE) was greater for the larger firms—probably due to the fact that many of the smaller firms have proportionately more employees than larger firms and proportionately less in net sales. One hundred eighteen firms (11.4%) reported either no operating income or negative operating income in 2001, and of these firms, 94 had fewer than 50 employees.

Results from the *Critical Technology Assessment* survey reveal clear distinctions based on firm size and provide more detailed information about the distinctive characteristics of smaller biotechnology companies engaged in biotech-related research and development. Such information should be useful in efforts to craft and implement public policies related to firms engaged in biotechnology.

Table 2.6: Financial Performance by Firm Size; Biotechnology and Entire Business, 2001 Totals ($ million)

Totals ($ million)	1–10	11–50	51–500	501–2,500	2,501–15,000	>15,000	TOTAL
Entire Business							
Net Sales	$410	$756	$15,531	$29,262	$123,336	$397,665	$566,985
COGS	$320	$442	$9,174	$13,326	$43,465	$227,490	$294,233
Operating Income	–$120	–$522	–$449	$4,699	$30,815	$66,094	$100,516
Total Capital	$100	$331	$2,192	$1,783	$6,936	$18,192	$29,536
R&D Expenditures	$162	$930	$5,181	$4,911	$15,052	$15,354	$41,590
Biotechnology Business							
Net Sales	$372	$515	$5,929	$10,457	$15,464	$17,733	$50,473
COGS	$295	$312	$3,438	$4,326	$4,635	$3,990	$16,997
Operating Income	–$115	–$520	–$1,506	$2,037	$3,699	$5,773	$9,368
Total Capital	$12	$308	$1,346	$1,009	$1,407	$2,162	$6,244
R&D Expenditurres	$163	$888	$4,612	$3,563	$3,735	$3,478	$16,441

Percentage of Total	1–10	11–50	51–500	501–2,500	2,501–15,000	>15,000	TOTAL
Entire Business							
Net Sales	0.09	0.17	3.52	6.63	27.95	61.62	100.00
COGS	0.13	0.18	3.78	5.50	17.93	72.47	100.00
Operating Income	–0.15	–0.65	–0.56	5.81	38.12	57.42	100.00
Total Capital	0.34	1.12	7.42	6.04	23.48	61.59	100.00
R&D Expenditures	0.39	2.24	12.46	11.81	36.19	36.92	100.00
Biotechnology Business							
Net Sales	0.74	1.02	11.75	20.72	30.64	35.13	100.00
COGS	1.74	1.83	20.23	25.45	27.27	23.48	100.00
Operating Income	–1.23	–5.55	–16.07	21.73	39.47	61.64	100.00
Total Capital	0.20	4.93	21.55	16.17	22.53	34.62	100.00
R&D Expenditures	0.99	5.40	28.05	21.67	22.72	21.16	100.00

Note: Percentage totals do not add up to 100% because of unknown data.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Table 2.7: Financial Indicators by Firm Size for Biotechnology Business, 2001

	≤500	>500
COGS as a percentage of net sales	59.3	29.7
Operating Income as a percentage of net sales	–31.4	26.4
Labor Productivity		
Net Sales/FTE	170,080	483,821
(Net Sales-COGS)/FTE	69,144	340,287
Capital Intensity		
Capital Expenditures/Net Sales	24.4	10.5
Capital Expenditures/FTE	41,574	50,738
R&D Intensity		
R&D Expenditures/Net Sales	83.1	24.7
R&D Expenditures/FTE	141,346	119,439

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

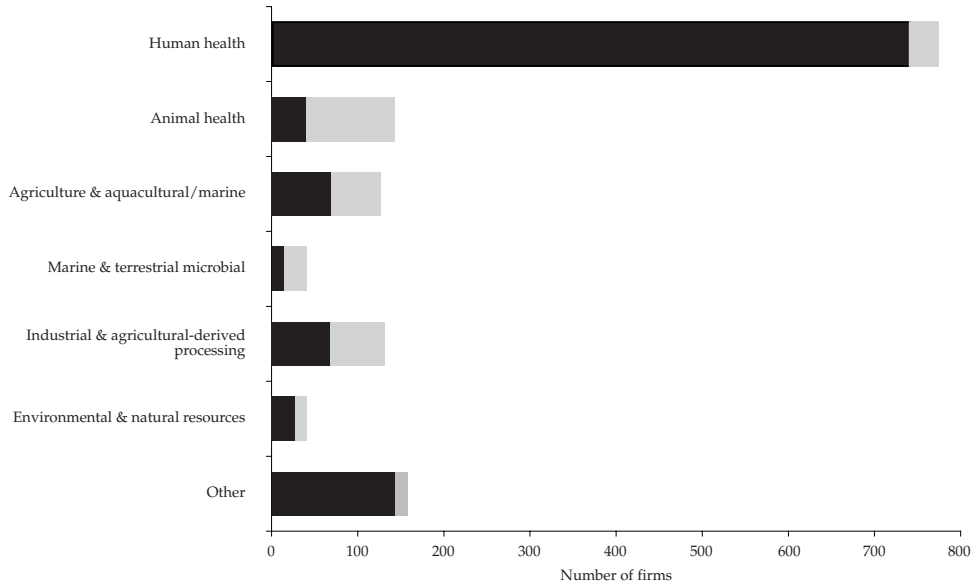
Chapter 3
Biotechnology Applications

In an effort to better understand the scope of biotechnology applications by U.S. industry, the *Critical Technology Assessment* survey asked respondents to provide information on the focus of their biotechnology-related lines of business by selecting one of eight categories.[30] Respondents were allowed to designate multiple "primary" and "secondary" areas of activity; they also were encouraged to provide written explanations of their work.

The *CTA* did not ask respondents to prioritize their responses, which are presented here. Therefore, information presented for any specific application category represents combined data of all respondents that identified that application as either a "primary" or "secondary" focus of their work; quantitative data are not additive across applications and should be evaluated carefully. As Figure 3.1 illustrates, more than half the data for some applications was provided by firms that indicated the area as a secondary area of biotech activity for their business.

This chapter is divided into seven biotechnology application categories: human health, animal health, agricultural and aquaculture/marine, industrial and agricultural-derived processing,

Figure 3.1: Biotechnology Activities Identified by Responding Companies



Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Technology in U.S. Industry,* p. vii, August 2002.

[30] The eight categories included human health, animal health, agriculture and aquaculture, marine and terrestrial microbial applications, industrial and agricultural processing, environmental remediation, natural resource recovery, and "other."

environmental remediation and natural resource recovery, marine and terrestrial microbial, and "other." It also includes a section that examines characteristics of respondents that indicated they have recently held defense contracts.[31]

Although presented data are application-specific, there also are similarities across all types of biotech activities. For example, regardless of the type of biotech application, the majority of firms have fewer than 50 employees and most of those employees have biotechnology-related responsibilities (Table 3.1). In addition, as noted in Chapter 2, there are striking differences in the financial pictures of small and large firms, with many smaller companies reporting negative average operating income. Data tables that present financial averages for each application by firm size category are presented in Appendix C.

Comparisons of financial averages across application areas are also instructive. For example, firms engaged in animal health applications appear to be the most financially robust in terms of average net sales, average operating income, and average capital expenditures (Table 3.2). For firms engaged in agricultural and aquacultural biotech activities, average operating income is negative, despite having one of the highest level of R&D intensity.

Each section follows a similar progression. First, information is presented that provides a snapshot of respondents whose biotechnology-related business lines are concentrated in that application.[32] This is followed by an explanation of the types of biotechnology activities and research identified by those firms, as well as the financial health of respondents' biotech business lines and their entire business, including estimates of comparative net sales and operating income, capital expenditures, and financial investments in research and development. Each application section concludes with information about reported sources of financing and government partnerships.

Human Health Applications

The *CTA* survey provides support for the common impression that human health (HH) is, by a large margin, the predominant focus of U.S. companies engaged in biotechnology. More than three-quarters of all companies responding to the survey (780 of 1,031) identified human health as either a primary or secondary focus of their biotechnology activities. In fact, the vast majority of these companies (747) indicated human health to be the primary application area; 33 other firms designated human health as a secondary focus. NAICS codes reported by respondents are presented in Appendix C.

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[31] *CTA*, question 39, page 16.

[32] Appendix C presents tables that provide information about firms' reported NAICS codes by application category, as well as data tables for each application category that present financial averages based on firm size.

Table 3.1: Distribution of Firms by Firm Size Categories and Relative Number of Biotech FTEs

Application	Percentage of firms, by firm size category (Percentage of FTEs with biotech-related responsibilities)					
	1–10	11–50	51–500	501–2,500	2,501–15,000	>15,000
Human Health	24.0 (75.2)	34.1 (77.6)	31.7 (69.1)	5.4 (50.2)	3.0 (24.2)	1.8 (3.4)
Animal Health	28.0 (74.7)	39.2 (75.9)	23.1 (53.6)	6.3 (73.2)	0	2.8 (8.4)
Agriculture and Aquaculture/ Marine	29.1 (71.5)	29.1 (74.2)	30.7 (50.4)	6.3 (29.1)	1.6 (18.8)	3.1 (2.7)
Environmental Remediation and Natural Resource Recovery	56.1 (67.5)	17.1 (59.3)	9.8 (55.41)	4.9 (35.7)	4.9 0	7.3 (3.9)
Marine and Terrestrial Microbial	41.5 (83.2)	22.0 (83.8)	14.6 (50.9)	9.8 (74.5)	4.9 (23.6)	7.3 (0.7)
Industrial and Agricultural-Derived Processing	22.9 (69.9)	29.0 (72.0)	28.2 (61.3)	6.9 (36.6)	6.1 (13.4)	6.9 (2.6)
Other	26.4 (63.2)	37.5 (69.1)	27.8 (47.5)	6.3 (58.7)	2.1 (35.3)	0

Table 3.2: Financial Performance of Biotechnology Businesses, by Application

Application	Employees (thousands)	Net Sales Avg ($ 000)	Operating Income Avg ($000)	Capital Expenditures Avg ($000)	Capital Expenditure Intensity (percent of net sales)	R&D Expenditures Avg ($ 000)	R&D Intensity (percent of net sales)
Human Health	151	65,326	12,876	8,368	12.5	21,612	33.4
Agricultural and Aquacultural/Marine	116	28,341	–730	2,747	9.5	9,877	35.2
Animal Health	180	124,025	37,227	18,287	14.3	24,714	19.9
Industrial and Agricultural-Derived Processing	190	52,504	5,557	4,829	9.2	16,874	32.1
Marine and Terrestrial Microbial	209	61,347	7,700	4,486	7.1	14,900	23.6
Environmental Remediation and Natural Resource Recovery	149	30,541	2,876	2,277	7.7	11,532	36.7
Other	93	23,308	526	3,373	13.5	7,682	30.9

Respondents reside in 44 states, with 14 states[33] accounting for nearly 85% of firms. California is particularly prominent; it was cited as the location for 29% of HH respondents; Massachusetts and Maryland have sizable concentrations, representing 10% and 9%, respectively.

Mirroring the larger sample of respondents, most HH application companies are comparatively young, and there is minimum foreign ownership. Data indicate that 67% were established since 1990, but a few (4%) were in business prior to 1950. Eighty-one percent of HH respondents own their own companies; 65% of the others are owned by U.S. companies. Companies from Germany, Canada, France, the United Kingdom, and Switzerland are the most frequent foreign owners.

Human Health (HH) Respondents' Biotechnology Applications and Activities

Recent statistics published by the Biotechnology Industry Organization (BIO)[34] indicate that more than 155 biotechnology drugs and vaccines have received regulatory approval from the Food and Drug Administration (FDA) to date (about 70% of these in the last six years). Further, more than 370 biotech drug products and vaccines are currently in clinical trials—products that are targeting hundreds of diseases, such as various cancers, Alzheimer's disease, heart disease, diabetes, multiple sclerosis, AIDS, and arthritis. Biotechnology is also responsible for hundreds of new medical diagnostic tests, such as those that help ensure a safe blood supply and others that enable early detection of diseases, and thereby contribute to successful treatment.

Survey respondents indicated that their research and development activities in human health are broadly directed at therapeutics (e.g., biopharmaceuticals such as biotechnology-derived proteins, antibodies and enzymes, and genetic therapies), medical diagnostics (e.g., tests for specific gene or protein markers), and preventives (e.g., new vaccines developed through recombinant DNA methods). Of 780 HH respondents, 70% indicated that their application activities were broadly directed at therapeutics, 42% indicated medical diagnostics, and 21% indicated the area of preventives.

In general, HH firms reported a greater focus on research activities than on more downstream activities such as product and process development or clinical trials. Relatively few companies indicated approved products or processes in the marketplace (Table 3.3). More than one-third of respondents (36%–45%) indicated that they were active in research activities related to such areas as gene probes/DNA markers and improved methods for DNA analysis, cell culturing/manipulation, and extractions, separations, and purifications. With the exception of diagnostic tests and antibiotics, development, preclinical, and clinical trial activities were mentioned about half as frequently. Approved and marketed products or processes generally were indicated by less than 10% of the companies, although drug design and delivery had a strong showing across the research-to-market spectrum of product development.

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[33] California, Massachusetts, Maryland, North Carolina, New Jersey, Pennsylvania, New York, Texas, Washington, Colorado, Virginia, Connecticut, Michigan, and Wisconsin.

[34] Biotechnology Industry Organization, "Biotechnology Industry Statistics," posting as of July 2003 (http://www.bio.org/er/statistics.asp).

Table 3.3: Biotechnology Activities of Respondents Working in Human Health Applications

	Conduct research on/in (%)	Development, pre-clinical trials, or confined field tests (%)		Clinical trials, or unconfirmed release assessments (%)	Approved, marketed, or in production (%)	
		Product(s)	Process(es)		Product(s)	Process(es)
DNA-based						
Gene probes, DNA markers	36	11	6	5	6	3
Bioinformatics	32	5	4	2	2	1
Genomics, pharmacogenetics	33	7	5	3	3	2
DNA sequencing/synthesis/ amplification, genetic engin.	43	13	9	5	5	3
Biochemistry/Immunology						
Vaccines/immune stimulants	22	15	9	9	2	1
Drug design & delivery	41	28	13	15	5	2
Diagnostic tests, antibiotics	31	16	8	9	11	7
Synthesis/sequencing of proteins and peptides	31	11	6	5	2	2
Cell receptors/signaling, structural biology	31	8	4	3	2	1
Combinatorial chemistry, 3-D molecular modelling	21	6	3	1	1	0
Biomaterials	11	7	4	3	3	2
Microbiology, virology, microbial ecology	25	11	6	6	5	5
Bioprocessing-based						
Culturing/manipulation of cells, tissues, embryos	41	15	12	7	6	5
Extractions, purifications, separations	37	17	14	8	9	7
Fermentation, bioprocessing, biotransformation	25	13	12	8	6	5
Environmental						
Bioleaching, biopulping, biobleaching, biodesulfurization	1	1	1	0	0	0
Bioremediation, biofiltration	1	0	1	0	0	0
Other	6	3	2	1	2	1

776 of the 780 companies in this application category responded to this question.

Cited figures will not in most cases add up to 100%, as the responding companies could list multiple activities.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

HH Respondent's Economic Characteristics

The 780 companies that selected human health applications as a primary or secondary focus of their biotechnology activities represented between 90% and 98% of total financial activity reported by all survey respondents.[35] HH firms reported about 117,000 employees with biotechnology-related responsibilities.[36] In 2001, HH firms' biotech business lines accounted for $46.7 billion in net sales, $9.2 billion in operating income, $5.8 billion in capital expenditures, and $15.6 billion in R&D expenditures (Table 3.4). However, analysis reveals that there is considerable diversity in the economic experiences of HH firms based on total company employment. For example, figures for average operating income in 2001 indicate an average range of $52 million to $412 million for larger companies, but a negative (deficit) ranging from minus $0.6 million to minus $7 million for the smaller companies. (See Appendix C for detailed financial tables for HH firms by firm size category.) Unsurprisingly, some of the larger companies with a presence in human health-related biotechnology applications also have business interests and existing, successful product portfolios in markets such as traditional pharmaceuticals.

Although biotechnology is a modest fraction of the full business activities of HH companies, accounting for 15% of annual net sales, 14% of operating income, 26% of capital investment, 40% of R&D expenditures, and 14% of employment, analysis reveals that R&D and capital intensity[37] of respondents' biotech business lines were much greater than for their entire business (33.4% and 12.5%, compared to 8.9% and 5.1%, respectively).

Exports

Export markets are an important addition to business revenues for some HH firms. Of the 646 companies providing data, 253 indicated that they exported biotechnology products or services in 2001. Exports' importance varied for these firms, ranging as high as 100% of net revenues, although the average was about 10%.[38] HH firms reported that the United Kingdom and countries in the European Union (EU) were the most common foreign markets (see Chapter 7). Japan and Canada were also prominent destinations for HH biotech exports in 2001.

Government Partnerships and Collaborations

Fifty-eight percent of HH firms indicated their participation in one or more federal programs that seek to facilitate cooperative research, technology transfer, or small business innovation/development activities. The most prominent program (for 37% of responding companies) was

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[35] Current dollars. These proportions provide an approximation of the prominence of HH applications, but care is needed in interpretation, as 33 firms indicated that they consider at least one other area of biotech activity to be "primary" for their business.

[36] Inclusive of all scientific/technical, production, and administrative personnel.

[37] R&D intensity is calculated as a ratio of R&D to net sales. Capital intensity is a ratio of capital expenditures to net sales.

[38] *CTA,* question 30, page 12.

Table 3.4: Economic and Business Statistics for Respondents Working in Human Health Applications, 2001

	Companies identifying application as primary		Companies identifying application as primary or secondary		All biotech companies reporting in this survey	
		Cases reporting		*Cases reporting*		*Cases reporting*
Number of businesses in application	**747**		**780**		**1,031**	
Employment (FTEs)						
Entire business	746,829	746	852,120	779	1,134,879	1,030
Biotech activities	107,604	747	117,474	780	130,305	1,031
Net Sales ($ thousand)						
Entire business	$415,768,300	708	$442,756,800	737	$566,985,000	976
Biotech activities	$44,058,280	684	$46,708,060	715	$50,472,720	942
Operating Income ($ thousand)						
Entire business	$79,779,690	705	$84,841,150	734	$100,516,300	970
Biotech activities	$9,176,734	683	$9,196,229	714	$9,367,822	938
Capital Expenditures ($ thousand)						
Entire business	$20,960,060	687	$22,751,730	716	$29,535,620	953
Biotech activities	$5,542,429	668	$5,848,923	699	$6,244,325	913
R&D Expenditures ($ thousand)						
Entire business	$37,323,210	697	$39,520,640	725	$41,590,290	951
Biotech activities	$14,751,780	692	$15,604,130	722	$16,440,990	936
Patents						
Total active	19,750	671	21,747	702	23,992	921
Applications pending	28,262	681	31,240	714	33,131	928
Exports						
Number of firms exporting	232	617	253	646	388	869

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry*, August 2002.

the Small Business Innovation Research (SBIR) grants.[39] About 15% of firms indicated participation in R&D activities conducted through contract with a federal agency; 12% had a Cooperative Research and Development Agreement (CRADA)[40] with a federal laboratory; and grants

[39] As established by the Small Business Innovation Act of 1982 (P.L. 97-219). The Act requires the federal agencies to fund small business R&D that is directed toward innovation with commercial prospect and that is related to the agency's missions.

[40] CRADAs are intended to facilitate and encourage federal labs to participate in research, development, and demonstration partnerships with U.S. industry or other nonfederal parties for the purpose of advancing promising technologies toward commercialization. The authority was first established by the Federal Technology Transfer Act of 1986 and subsequently modified by the National Competitiveness and Technology Transfer Act of 1989.

through the Small Business Technology Transfer (STTR) Program[41] or licensing-in technology patented by a federal agency were each reported by about 6% of HH firms.

Future Business Strategies

Most HH companies provided information about the likelihood that they would pursue new strategic business initiatives in the immediate future. The vast majority of firms anticipated significant new activities; only 3% of the 780 HH firms indicated no intent to pursue new business initiatives in the next several years. As shown in Table 3.5, licensing-out technology was the most frequently cited initiative (mentioned by 60% of the companies). Other initiatives cited by more than half of the companies were expanding operations (54%), entering product trials (51%), and licensing-in technology (51%). Other frequently cited strategies included refocusing R&D activities and product development (45% and 39%, respectively), launching a new product (38%), increasing recruitment efforts for U.S. workers (36%), outsourcing production (27%), forming a joint venture (24%), and expanding into foreign markets (22%).

Agricultural and Aquaculture/Marine Applications

Twelve percent of survey respondents (128) indicated agriculture and aquaculture/marine (AAM) biotechnology as either their primary or secondary focus;[42] 70 of these indicated that this area was their primary biotech-related business. Fifty firms that reported AAM applications as their secondary focus also were primarily involved in human health applications of biotechnology.[43] AAM companies accounted for 12% of all survey respondents and 11.4% of total biotech employees (14,900). However, they accounted for only 6.4% of biotech net sales ($3.2 billion)[44] and 4.9% of biotech capital expenditures ($308 million).

Almost half of AAM respondents (48%, or 62) were established in the 1990s. The period 1997–1999 saw the greatest growth in establishment of new firms, when 34 companies (27%) were established. About 38% of respondents were established in prior years; 27 firms were established in the 1980s and 21 prior to the 1980s.

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[41] The STTR Program was established by the Small Business Technology Transfer Act of 1992 (P.L. 102-564). STTR gives five major federal agencies the responsibility to sponsor cooperative R&D projects involving small companies and researchers in noncommercial organizations.

[42] Animal health and agricultural processing applications are covered in other sections of this chapter.

[43] Because of this overlap, data presented in Chapter 3 cannot be added to equal totals for the entire sample.

[44] An input/output analysis by Ernst & Young (2000), produced for the Biotechnology Industry Organization, found that agricultural biotech generated 21,900 jobs, $2.3 billion in revenues, and $1.4 billion in personal income. This result included contributions of companies supplying inputs to the industry or goods and services to employees.

Most survey respondents (73%) were not owned by another firm; only 25 indicated that they were owned entirely by another company. Of these, nine firms were entirely owned by a domestic firm, and nine firms were owned by a foreign company. Foreign ownership was concentrated in the United Kingdom (three) and Germany (two), with the other four owners identified as being companies in Denmark, Hungary, Japan, and the Netherlands. Ten companies indicated that they were partially owned, with three indicating partial ownership in the United States and two each in Ireland and Japan.

AAM companies were dispersed geographically, with the highest concentration of respondents located in California (20%), North Carolina (9%), Wisconsin (6%), New Jersey (6%), Iowa (5%), and Massachusetts (5%). These states account for about 52% of the AAM biotechnology respondents.

Table 3.5: Competitive Strategies of Respondents Working in Human Health Applications

Strategic Response to Business Conditions	Number of companies indicating this action	Percentage of companies responding
No change in strategic response	26	3.3
License-out technology	468	60.0
Expand operations	423	54.2
License-in technology	396	50.8
Enter product trials	398	51.0
Refocus R&D activities	348	44.6
Launch a new product	293	37.6
Refocus product development	300	38.5
Increase recruitment efforts for U.S. workers	276	35.4
Outsource production	208	26.7
Expand into foreign markets	169	21.7
Form a joint venture	190	24.4
Merge with other company	88	11.3
Acquire a company	85	10.9
Downsize operations	83	10.6
Recruit employees abroad	84	10.8
Establish facilities abroad	60	7.7
Establish additional R&D collaborations	1	0.1
Other	15	1.9
No response	6	0.8

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

AAM Respondents' Biotechnology Applications and Activities

The application of modern biotechnology methods to agriculture has been hailed as the next agricultural revolution, capable of sustaining agricultural production to meet the dietary needs of an expanding world population, as well as increasing demands for improved food and environmental quality. Moving biotechnology applications to marine "farming" (aquaculture) also promises to improve aquaculture production—a goal that has become more critical for meeting increased consumer demand as natural seafood stocks have dwindled.

Most commercial agricultural biotechnology products have production-enhancing traits that complement or replace traditional agricultural chemical inputs.[45] Crops generally are designed

[45] A U.S. Department of Agriculture report shows that private-sector investments in agricultural R&D were increasingly devoted to biologically related technologies. In 1960, plant breeding and animal health accounted for 6% of agricultural research expenditures, and by 1998, 24% of agricultural R&D expenditures were allocated to these applications. See Agricultural Resources and Environmental Indicators (AREI), No. AH722, Economic Research Service, USDA, Feb. 2002 at http://www.ers.usda.gov/publications/arei/arei2001/arei5_2DBGen.htm (viewed Aug. 2003).

to be herbicide-tolerant or pest-, virus-, or fungus-resistant. Biotechnology also is used to improve agronomic characteristics of crops, including crops that use nitrogen more efficiently or are developed to better tolerate stress, such as drought, alkaline soils, or frost.

In livestock production, biotechnology is being used to develop animals that have better growth and muscle mass and improved disease resistance (see following section about animal health applications), and that can utilize feed more efficiently. Biotechnology applications are also aiding in the development of better diagnostics to detect animal and plant diseases. Biotechnology applications in aquaculture will be able to produce larger fish with less feed, improve spawning, and reduce the time for fish to gain market weight.

The next phase of agricultural biotechnology products promises improved quality and end-user traits. Some examples of quality-enhanced foods that are being developed include foods with lower saturated fats, increased vitamin content, and improved flavor and shelf life. Additionally, plants and animals can be developed to produce specialty chemicals and pharmaceuticals.

Survey respondents were asked to provide information on their biotechnology activities. Of firms reporting that they specialize in AAM applications, biotechnology-related activities included product development and solutions to problems related to seed and plants (63%), livestock (41%), and aquaculture (16%). Eighty-four percent of these companies also responded that biotechnology was a central focus of their firm or division.

As with companies concentrating in other biotechnology applications, more AAM respondents were engaged in research than have products in unconfined release assessments. In fact, AAM firms reported the highest level of R&D intensity of any application area (see Table 3.2). While AAM firms participate in a wide variety of research and development activities, most were primarily conducting DNA-related research: 47% reported research in DNA sequencing/synthesis/amplification and genetic engineering, and 46% indicated work in gene probes and DNA markers (Table 3.6).

About one-third of AAM firms also indicated that they conducted research on extractions, purifications, and separations (35%); culturing/manipulation of cells, tissues, and embryos (34%); bioinformatics (32%); diagnostic tests and antibiotics (31%); and microbiology, virology, and microbial ecology (31%). A slightly higher percentage indicated significant research in fermentation, bioprocessing, and biotransformation (38%) and genomics and pharmacogenetics (38%).

Fewer firms reported having products approved, marketed, or in production. The leading area—indicated by 17% of respondents—was fermentation, bioprocessing, and biotransformation. Other areas included (in order of importance) gene probes and DNA markers; DNA sequencing/synthesis/amplification and genetic engineering; diagnostic tests and antibiotics; microbiology, virology, and microbial ecology; and extractions, purifications, and separations.

Table 3.6: Biotechnology Activities of Respondents Working in Agriculture and Aquaculture/Marine Applications

	Conduct research on/in (%)	Development, pre-clinical trials, or confined field tests (%)		Clinical trials, or unconfirmed release assessments (%)	Approved, marketed, or in production (%)	
		Product(s)	Process(es)		Product(s)	Process(es)
DNA-based						
Gene probes, DNA markers	46	14	9	6	12	7
Bioinformatics	32	10	7	2	3	2
Genomics, pharmacogenetics	38	12	6	2	4	3
DNA sequencing/synthesis/ amplification, genetic engin.	47	19	12	6	11	6
Biochemistry/Immunology						
Vaccines/immune stimulants	15	8	5	4	3	1
Drug design & delivery	18	8	4	2	0	0
Diagnostic tests, antibiotics	31	13	6	2	10	7
Synthesis/sequencing of proteins and peptides	24	5	5	2	2	2
Cell receptors/signaling, structural biology	17	5	2	2	2	2
Combinatorial chemistry, 3-D molecular modelling	13	4	2	0	4	1
Biomaterials	9	5	3	1	2	2
Microbiology, virology, microbial ecology	31	10	6	5	10	5
Bioprocessing-based						
Culturing/manipulation of cells, tissues, embryos	34	9	8	1	6	2
Extractions, purifications, separations	35	15	13	3	10	11
Fermentation, bioprocessing, biotransformation	38	14	11	3	17	13
Environmental						
Bioleaching, biopulping, biobleaching, biodesulfurization	3	0	0	0	0	0
Bioremediation, biofiltration	6	1	1	1	2	0
Other	7	5	2	0	3	2

127 of the 128 companies in this application category responded to this question.

Cited figures will not in most cases add up to 100%, as the responding companies could list multiple activities.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

AAM Respondents' Economic Characteristics

The financial performance of AAM companies resembles that of many other biotechnology applications in that operating income of biotechnology business lines is negative (minus $85 million),[46] but R&D and capital intensity are high. As shown in Table 3.7, R&D expenditures as a percentage of net sales for the biotech business segment were 37%, or about six times higher than for the entire business operation (6.2%). Similarly, capital expenditures as a percentage of net sales for the entire business operations of respondents were 4.3%, compared to 10.5% for the biotech business segment.

In comparison to the total survey population, AAM firms were active in biotech R&D, spending 6.9% of total reported biotech R&D expenditures and accounting for 12.1% of all active patents and 13.6% of pending applications. They also were active in technology licensing markets, especially related to patents and trade secrets.[47] Plant breeders' rights[48] were not the subject of technology transfer activities as often as patents and trade secrets, possibly because the latter offer greater intellectual property protection for a more diverse set of technologies than plants alone. AAM firms often licensed-in technologies from other companies, and they seemed to conduct a significant amount of technology transfer activities abroad. For example, there were 52 responses[49] indicating that patent rights were either acquired from, or granted to, foreign firms; there were 29 similar responses for trade secrets and plant breeders' rights.

Exports

Despite some market barriers (see below), AAM firms are participating in export markets. In 2001, 42% of AAM companies indicated that they exported biotechnology products or processes, compared to 46% for all survey respondents. These exports accounted for 26% of their net revenues on average. The markets that accounted for the largest average share of firms' export revenues were Canada (35%), Japan (28%), Brazil and other Latin American countries[50] (23%), Germany (20%), other EU countries (19%), the United Kingdom (18%), and Mexico (18%).

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[46] Despite negative operating income, firms are not operating without funds. These firms have positive operating income for their entire business operations ($9.3 billion), and employee licensing income, outside funding sources, and federal programs for their biotechnology research and development needs.

[47] *CTA*, question 35, page 14.

[48] Because merely possessing a biological invention, such as a new plant variety, provides the means to reproduce it, it is necessary to establish intellectual property protection. Protection allows plant breeders to capture some of their R&D investments, and thus motivates the development of plant varieties. In the United States, the Plant Patent Act of 1930 and the Plant Variety Protection Act of 1970 established plant breeders' rights. However, recently patents have been granted for some new plant varieties.

[49] Note that one firm could provide more than one response to this question.

[50] Not including Mexico.

Table 3.7: Economic and Business Statistics for Respondents Working in Agriculture and Aquaculture/Marine Applications, 2001

	Companies identifying application as primary		Companies identifying application as primary or secondary		All biotech companies reporting in this survey	
		Cases reporting		*Cases reporting*		*Cases reporting*
Number of businesses in application	**69**		**128**		**1,031**	
Employment (FTEs)						
Entire business	163,859	69	208,306	127	1,134,879	1,030
Biotech activities	5,844	69	14,881	128	130,305	1,031
Net Sales ($ thousand)						
Entire business	$48,221,260	63	$51,698,620	121	$566,985,000	976
Biotech activities	$1,538,733	59	$3,230,926	114	$50,472,720	942
Operating Income ($ thousand)						
Entire business	$8,953,845	65	$9,257,443	121	$100,516,300	970
Biotech activities	–$71,455	61	–$84,732	116	$9,367,822	938
Capital Expenditures ($ thousand)						
Entire business	$1,972,147	65	$2,229,801	119	$29,535,620	953
Biotech activities	$135,565	61	$307,668	112	$6,244,325	913
R&D Expenditures ($ thousand)						
Entire business	$2,373,842	62	$2,958,814	117	$41,590,290	951
Biotech activities	$639,644	61	$1,135,859	115	$16,440,990	936
Patents						
Total active	1,673	57	2,910	112	23,992	921
Applications pending	2,395	62	4,506	114	33,131	928
Exports						
Number of firms exporting	26	57	54	107	388	869

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Government Partnerships and Collaborations

AAM firms are active participants in federal programs supporting small business and cooperative research, and technology transfer. About 35% of these companies received Small Business Innovation Research (SBIR) grants and 16% participate in other grants programs. Companies also reported participating in contracts (15%), Cooperative Research and Development Agreements (13%), and in-licensing from federal agencies (8%).

Competitive Concerns and Future Business Strategies

Survey respondents were asked to indicate barriers that could impede the advancement of their biotechnology research or product commercialization.[51] In response, the largest number of AAM companies indicated the regulatory approval process and costs (21 firms), research costs (19 firms), and public acceptance/ethical considerations (18 firms). Other barriers included unfair foreign laws (13 firms), access to start-up capital (13 firms), and patent rights held by third parties (12 firms).

Responses from AAM firms differed somewhat from those of the survey sample as a whole, particularly with respect to companies' high level of concern about public acceptance/ethical considerations and unfair foreign laws (see Chapter 7).

This perspective reflects questions that have been raised, especially internationally, about genetically modified organisms. Compared to other biotechnology applications examined in this report, development and application of agriculture/aquaculture biotechnologies has met with increasing concern about potential effects on the environment and food safety. These concerns, which are largely focused on engineering of input-reducing or production-enhancing traits, has led to increased regulatory requirements and uncertain market demand. Foreign markets—especially the EU and Japan—have been particularly affected, and many are requiring the segregation and labeling of food products that are produced using genetically modified organisms.

Despite these concerns, the adoption of genetically modified crops has expanded since widespread introduction in 1996 of genetically engineered crops such as herbicide-tolerant and Bt[52] crops. By 2001, 68% of soybean, 55% of cotton, and 8% of corn acres were planted with herbicide-tolerant varieties in the United States. For Bt crop varieties, 19% of corn and 37% of cotton acres were planted with these varieties.[53] Adoption of genetically modified crops also has been increasing in other countries, such as Argentina, Canada, and China.[54]

Seventy-eight percent of AAM respondents expect their competitive prospects to improve greatly or somewhat. To boost their competitive prospects, the top three business strategies that firms plan to employ in 2002 and 2003 are licensing-out technology (52%), acquiring technology (49%), and refocusing R&D activities (49%) (Table 3.8). A relatively high proportion of companies also indicated that they planned to expand operations (46%), launch a new product (43%), and refocus product development (43%). Additionally, 54% of AAM respondents are contemplating expanding their facilities or infrastructure. Fifty-six percent of firms are considering contracting with U.S. firms or facilities, while 34% are considering contracting with foreign firms or

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[51] About 25% of AAM respondents (128) answered this question.

[52] *Bacillus thuringiensis* (Bt) is toxic to certain pests. It can be applied to plants topically and also has been genetically incorporated into plants.

[53] See http://www.ers.usda.gov/Briefing/Biotechnology/ (viewed Sept. 2003).

[54] International Service for the Acquisition of Agri-biotech Applications. See http://www.isaa.org/ (viewed Sept. 2003).

facilities. For the entire survey sample, only 26% of companies indicated that they are considering contracting with foreign entities.

Animal Health

The broad objectives of biotechnology applications related to animal health (AH) are largely the same as in human health (HH) applications—applying advances in genetics and molecular biology to discover and create new and more powerful therapeutic products (proteins, antibodies, enzymes, genetic therapies), diagnostic tools (e.g., for gene or protein markers of disease conditions), and preventive measures such as vaccines. In addition, biotechnology is providing powerful new tools for improving farm animal breeding programs, including genetic mapping methods to identify both disease-resistant animals and certain specific genes related to health weaknesses and defects.

Forty-one of 1,031 survey respondents (4%) indicated that animal health was a primary focus; another 103 firms identified animal health applications as a secondary focus. The 144 companies with either a primary or secondary focus on animal health applications represent about 14% of survey firms and account for about 15% of net sales and 17% of capital expenditures.

Table 3.8: Competitive Strategies of Respondents Working in Agriculture and Aquaculture/Marine Applications

Strategic Response to Business Conditions	Number of companies indicating this action	Percentage of companies responding
No change in strategic response	10	7.8
License-out technology	67	52.3
Expand operations	59	46.1
License-in technology	63	49.2
Enter product trials	48	37.5
Refocus R&D activities	63	49.2
Launch a new product	55	43.0
Refocus product development	55	43.0
Increase recruitment efforts for U.S. workers	42	32.8
Outsource production	32	25.0
Expand into foreign markets	43	33.6
Form a joint venture	37	28.9
Merge with other company	14	10.9
Acquire a company	24	18.8
Downsize operations	18	14.1
Recruit employees abroad	20	15.6
Establish facilities abroad	13	10.2
Establish additional R&D collaborations		0.0
Other	6	4.7
No response	2	1.6

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

As noted above, most AH firms also focus on HH applications. Fifteen of the 41 companies identifying animal health as a primary focus also identified human health as a primary focus, and 90% of the companies identifying animal health as a secondary focus identified human health as a primary focus (93 of 103).

Almost half of all AH firms are more than 20 years old; about 10% reported that they were established before 1970 and another 40% during the 1970s and 1980s. Half of all AH respondents have emerged since 1990. About 20% of AH respondents were located in California, with other firms distributed across 17 other states.

Survey results indicated that 81% of AH firms were self-owned. Fifteen of the remainder were either majority-owned or fully owned by U.S. companies, while six were owned by companies from Australia, Canada, Japan, the Netherlands, or the United Kingdom.

Animal Health Respondents' Biotechnology Applications and Activities

While the regulatory process for AH products differs significantly from that for HH products, there are similarities in terms of technologies employed, research activities, and product development. Responses to questions about the types of current technical activities indicate that most AH firms' biotech-related activities are focused on downstream activities such as product and process development and clinical trials. The Biotechnology Industry Organization (BIO) indicates that biotechnology-based products and services for animal health presently amount to several billion dollars annually and appear likely to double in the next several years.[55] At the end of 2001, some 2,494 different biologics were available for use against 197 different animal diseases. AH firms reported 4,506 patents pending, 13.6% of the total reported by *CTA* respondents.

Company research activities are wide-ranging. The most frequently cited areas were gene probes and DNA markers; DNA sequencing/synthesis/amplification; vaccines and immune stimulants; diagnostic tests and antibiotics; culturing and manipulation of cells and tissues; microbiology and virology; fermentation and bioprocessing; and improved methods for extractions, separations, and purifications—each cited by 33% to 48% of companies (Table 3.9).

Between about one-quarter and one-third of AH firms indicated developmental and pre-clinical trial work in vaccines and immune stimulants; diagnostic tests and antibiotics; and methods for extractions, separations, and purifications. Vaccines and immune stimulants were the most frequently cited area for current clinical trials; they were mentioned by 20% of AH respondents.

In terms of approved, marketed, or in-production products and processes, AH firms have a strong showing in seven product categories and four process areas. Between 10% and 17% of companies indicated activity at this stage—most in areas of bioprocessing.

AH Respondents' Economic Characteristics

For their biotech business lines, AH survey respondents reported $16.7 billion in net sales in 2001, $5.0 billion in operating income, $2.4 billion in capital expenditures, and $3.3 billion in R&D expenditures (Table 3.10). However, firms that identified animal health as their primary application focus account for only 1% to 3% of these totals.

Biotechnology is only a modest fraction of overall company activities for the larger companies, but is a central—or exclusive—activity for smaller companies. In addition, biotech business

[55] Biotechnology Industry Organization, "Agricultural Production Applications," July 2003. (http://www.bio.org/er/agriculture.asp).

Table 3.9: Biotechnology Activities of Respondents Working in Animal Health Applications

	Conduct research on/in (%)	Development, pre-clinical trials, or confined field tests (%)		Clinical trials, or unconfirmed release assessments (%)	Approved, marketed, or in production (%)	
		Product(s)	Process(es)		Product(s)	Process(es)
DNA-based						
Gene probes, DNA markers	37	16	10	7	9	5
Bioinformatics	26	8	6	4	5	3
Genomics, pharmacogenetics	29	12	6	4	6	3
DNA sequencing/synthesis/ amplification, genetic engin.	42	18	14	7	10	8
Biochemistry/Immunology						
Vaccines/immune stimulants	43	30	17	20	10	4
Drug design & delivery	30	17	12	9	5	5
Diagnostic tests, antibiotics	48	24	15	8	15	11
Synthesis/sequencing of proteins and peptides	27	8	5	3	3	2
Cell receptors/signaling, structural biology	23	7	3	3	3	2
Combinatorial chemistry, 3-D molecular modelling	14	5	1	1	3	1
Biomaterials	12	4	4	1	1	1
Microbiology, virology, microbial ecology	38	17	7	10	15	8
Bioprocessing-based						
Culturing/manipulation of cells, tissues, embryos	34	15	13	7	11	10
Extractions, purifications, separations	45	24	19	10	17	15
Fermentation, bioprocessing, biotransformation	33	15	15	8	15	13
Environmental						
Bioleaching, biopulping, biobleaching, biodesulfurization	4	1	1	1	0	0
Bioremediation, biofiltration	3	1	1	0	0	0
Other	8	3	1	1	2	0

143 of the 144 companies in this application category responded to this question.

Cited figures will not in most cases add up to 100%, as the responding companies could list multiple activities.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Table 3.10: Economic and Business Statistics for Respondents Working in Animal Health Applications, 2001

	Companies identifying application as primary		Companies identifying application as primary or secondary		All biotech companies reporting in this survey	
		Cases reporting		*Cases reporting*		*Cases reporting*
Number of businesses in application	**41**		**144**		**1,031**	
Employment (FTEs)						
Entire business	8,339	40	181,736	143	1,134,879	1,030
Biotech activities	4,115	41	25,969	144	130,305	1,031
Net Sales ($ thousand)						
Entire business	$5,798,029	41	$82,559,700	138	$566,985,000	976
Biotech activities	$1,045,781	38	$16,743,338	135	$50,472,720	942
Operating Income ($ thousand)						
Entire business	$970,680	38	$15,018,100	137	$100,516,300	970
Biotech activities	$97,913	37	$4,988,393	134	$9,367,822	938
Capital Expenditures ($ thousand)						
Entire business	$247,264	38	$5,115,800	136	$29,535,620	953
Biotech activities	$90,787	35	$2,395,580	131	$6,244,325	913
R&D Expenditures ($ thousand)						
Entire business	$567,876	38	$6,890,544	136	$41,590,290	951
Biotech activities	$245,239	37	$3,336,405	135	$16,440,990	936
Patents						
Total active	859	33	3,381	131	23,992	921
Applications pending	507	32	3,562	128	33,131	928
Exports						
Number of firms exporting	26	34	70	124	388	869

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

lines had higher R&D and a capital intensity (as measured as a percentage of net sales) that was more than twice as high as overall business operations. For biotech business lines, R&D intensity was 19.9% and capital intensity was 14.3%, compared to 8.3% and 6.1% for all business. As with other types of biotech applications, firm size characteristics reveal other differences as well, with smaller firms generally reporting negative average operating incomes (see tables in Appendix C).

Exports

Seventy firms provided information about their export activities. For these companies, exports' share of annual net revenue averaged 15%, and in some cases, it was as high as 100% of net revenue. Canada is the leading export market for firms that indicated AH as a primary business

focus. Latin America and Japan were also noted as important markets. For all AH firms, the United Kingdom and the EU were cited by the most respondents.

Government Partnerships and Collaborations

Just over two-thirds (67%) of AH firms participated in one or more federal programs that seek to facilitate cooperative research, technology transfer, or small business innovation and development activities. Survey data indicate that about 40% of respondents have received Small Business Innovation Research (SBIR) grants, about 21% of firms conduct part of their R&D activities through a contract with a federal agency, and 18% had a Cooperative Research and Development Agreement (CRADA) with a federal laboratory. Licensing-in technology patented by a federal agency was noted by about 11% of firms and Small Business Technology Transfer (STTR) grants by about 10%.

Future Business Strategies

Most AH respondents (96%) indicated that they plan to pursue strategic business initiatives in the immediate future. As shown in Table 3.11, licensing-out technology was the most frequently cited initiative (mentioned by about 58% of the companies). Other initiatives cited by more than half of the companies were expanding operations (54%), licensing-in technology (53%), and launching new products (53%). Also frequently cited were entering product trials (49%) and refocusing R&D activities and product development (about 48% each), outsourcing production (33%), increasing recruitment efforts for U.S. workers (31%), expanding into foreign markets (31%), and forming a joint venture (28%).

Table 3.11: Competitive Strategies of Respondents Working in Animal Health Applications

Strategic Response to Business Conditions	Number of companies indicating this action	Percentage of companies responding
No change in strategic response	6	4.2
License-out technology	84	58.3
Expand operations	78	54.2
License-in technology	76	52.8
Enter product trials	71	49.3
Refocus R&D activities	70	48.6
Launch a new product	76	52.8
Refocus product development	69	47.9
Increase recruitment efforts for U.S. workers	45	31.3
Outsource production	48	33.3
Expand into foreign markets	45	31.3
Form a joint venture	40	27.8
Merge with other company	15	10.4
Acquire a company	21	14.6
Downsize operations	19	13.2
Recruit employees abroad	19	13.2
Establish facilities abroad	16	11.1
Establish additional R&D collaborations	0	0.0
Other	4	2.8
No response	0	0.0

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Industrial and Agriculture-derived Processing

About 12.8% of the survey population (132 companies) indicated that "industrial and agriculture-derived processing" (IAP) applications were either a primary or secondary focus of their business activities.[56] Of these, 110 respondents indicated that biotechnology is a central activity of their firm or division.[57] In terms of number of respondents, this application was one of the largest outside of "human health" and "other" applications; 69 respondents (6.7% of the survey sample) indicated that this application was their primary focus of activity.

More IAP respondents reported foreign ownership of companies than was the case for firms in any other application. France, Germany, the United Kingdom, and Japan were each cited as full owners of three firms; Japan and Ireland were cited as partial owners of two companies; and two respondents cited full ownership by Danish and Swedish concerns.

Thirty-one IAP respondents (23%) are located in California, followed by New Jersey and Wisconsin, with 10 companies each. Illinois, Texas, North Carolina, Pennsylvania, and Michigan were cited by at least 5% of IAP companies responding to the survey.

Biotechnology Applications and Activities

Biotechnology applications defy attempts to categorize them easily and spill across definitional boundaries that would restrict them to a particular industry. The application of biotechnology to IAP is illustrative. Many IAP products are created by applying natural or engineered microbes to products in order to extend shelf life, enhance nutritional characteristics, or preserve or create foods or industrial products. In response to a question asking IAP respondents to specify whether their biotech-related activities centered in food processing, specialty chemicals such as amino acids, or other commodity chemicals and applications, 12% indicated all three areas.[58] However, about 55% indicated a focus on specialty chemicals, while 40% specified food processing, and 34% selected other IAP applications.

As might be expected, IAP companies engage in many areas of research and have a strong presence in a variety of biotechnology products and processes that have been approved and are on the market (Table 3.12). Data also indicate that companies may be undertaking research in some relatively new areas such as bioinformatics.

In the IAP application area, as in all others, survey respondents reported more pending U.S. patent applications (5,146) than are currently held in company portfolios (4,410). These represented about 16% and 19% of total reported patents. Data indicate that respondents acquire

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[56] Analysis presented in this section is based on combined responses for the 132 respondents that indicated this application as either a primary or secondary focus of business activity, unless otherwise noted.

[57] *CTA*, question 7, page 3.

[58] *CTA*, page viii.

Table 3.12: Biotechnology Activities of Respondents Working in Industrial and Agriculture-derived Processing Applications

	Conduct research on/in (%)	Development, pre-clinical trials, or confined field tests (%)		Clinical trials, or unconfirmed release assessments (%)	Approved, marketed, or in production (%)	
		Product(s)	Process(es)		Product(s)	Process(es)
DNA-based						
Gene probes, DNA markers	45	13	9	5	11	5
Bioinformatics	34	9	8	4	4	1
Genomics, pharmacogenetics	37	12	10	4	5	2
DNA sequencing/synthesis/ amplification, genetic engin.	53	22	17	9	11	8
Biochemistry/Immunology						
Vaccines/immune stimulants	20	13	9	6	2	1
Drug design & delivery	22	13	9	5	3	2
Diagnostic tests, antibiotics	34	16	8	5	11	6
Synthesis/sequencing of proteins and peptides	33	13	8	5	7	3
Cell receptors/signaling, structural biology	25	7	5	4	4	3
Combinatorial chemistry, 3-D molecular modelling	18	7	5	2	4	2
Biomaterials	20	12	8	4	5	4
Microbiology, virology, microbial ecology	42	17	11	7	12	10
Bioprocessing-based						
Culturing/manipulation of cells, tissues, embryos	36	17	10	7	10	6
Extractions, purifications, separations	50	23	19	8	16	12
Fermentation, bioprocessing, biotransformation	47	23	21	10	25	18
Environmental						
Bioleaching, biopulping, biobleaching, biodesulfurization	8	2	2	1	1	1
Bioremediation, biofiltration	9	2	2	0	0	1
Other	5	2	2	0	1	2

132 of the 132 companies in this application category responded to this question.

Cited figures will not in most cases add up to 100%, as the responding companies could list multiple activities.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

more patents from domestic firms than they grant to either domestic or foreign firms, although they grant more trade secrets than they acquire.

IAP Respondents' Economic Characteristics

In 2001, IAP respondents accounted for about 19% of all reported biotech employees, 12.3% of reported net sales, 9.1% of capital expenditures, and 12.1% of reported R&D expenditures (Table 3.13). This is one of only two biotechnology applications that reported positive operating income ($69.4 million) for primary companies' biotech business lines in 2001. Operating income for all IAP respondents' entire businesses in 2001 was $40.6 billion; biotech-related activities accounted for 1.6% of this amount.

In 2001, biotech-related R&D accounted for 1.5% of all R&D expenditures for IAP companies. Biotech R&D intensity (as measured by the ratio of biotech R&D expenditures to net sales) was 32% for IAP respondents, compared to 6.4% for respondents' entire businesses. Capital intensity was also greater for biotech business lines than for entire IAP businesses in 2001: 9.2% compared to 5.2%. Biotech capital expenditures accounted for 5.2% of IAP companies' total 2001 capital expenditures.

Exports

As noted below, 36.4% of respondents plan to expand into new foreign markets. Currently about 60% of primary IAP companies export to a geographically diverse group of countries. Of 162 responses to a survey question inquiring about export markets, 26% of responses (42) identified Japan, China, Korea, and other Asian countries; 36% named EU countries such as France (11) and Germany (13); 15 cited the United Kingdom; and 17 cited Canada. Other foreign markets for IAP respondents included Brazil, Australia, India, and Mexico.

Government Partnerships and Collaborations

According to survey data, most IAP companies use in-house or parent firm financing to fund their biotechnology research; of 84 responses, about 60% cited these as sources of funding in 2001. However, venture capital and angel investing are also important (about 19% of responses), as are federal loans and grants (13%). Many of these loans and grants originate from the United States Department of Agriculture (USDA), the Department of Energy (DOE), the Department of Defense (DOD), or the National Institutes of Health (NIH). Small Business Innovation Research (SBIR) loans are particularly important for smaller IAP companies; about 21% of respondents who identified their participation in federal programs cited SBIRs. IAP respondents also indicated that they participate with federal laboratories' "Work for Others" and CRADA technology transfer programs.

Future Business Strategies

Although about 14% of respondents indicated plans to downsize operations, 53% plan to expand operations, and 36% plan to expand into foreign markets. In fact, about 78% of IAP respondents said they expected near-term business prospects to improve "greatly" or "some-

Table 3.13: Economic and Business Statistics for Respondents Working in Industrial and Agriculture-derived Processing Applications, 2001

	Companies identifying application as primary		Companies identifying application as primary or secondary		All biotech companies reporting in this survey	
		Cases reporting		*Cases reporting*		*Cases reporting*
Number of businesses in application		**69**		**132**		**1,031**
Employment (FTEs)						
Entire business	198,811	68	432,581	131	1,134,879	1,030
Biotech activities	8,070	69	25,082	132	130,305	1,031
Net Sales ($ thousand)						
Entire business	$69,578,180	64	$209,308,400	123	$566,985,000	976
Biotech activities	$1,673,053	60	$6,195,428	118	$50,472,720	942
Operating Income ($ thousand)						
Entire business	$9,792,001	65	$40,585,750	123	$100,516,300	970
Biotech activities	$69,446	60	$655,679	118	$9,367,822	938
Capital Expenditures ($ thousand)						
Entire business	$2,520,948	65	$10,863,310	122	$29,535,620	953
Biotech activities	$145,870	61	$569,878	118	$6,244,325	913
R&D Expenditures ($ thousand)						
Entire business	$854,409	65	$13,407,710	121	$41,590,290	951
Biotech activities	$294,603	62	$1,991,142	118	$16,440,990	936
Patents						
Total active	1,191	64	4,410	122	23,992	921
Applications pending	1,377	60	5,146	117	33,131	928
Exports						
Number of firms exporting	38	63	71	122	388	869

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

what," and all but eight have developed new near-term competitive strategies.[59] For more than 50% of IAP firms, strategies focus on product and process development, either by refocusing product development and R&D, or launching a new product (Table 3.14).[60] As with other types of biotechnology companies, technology licensing is an important strategic activity for companies working in IAP applications: 53% indicated that they plan to license their technology to other firms in the near future, while about 48% plan to acquire technology through licensing arrangements. More than one-third (35%) are contemplating joint ventures (which are often

[59] Based on 132 responses to question 33 of the *CTA*. Five companies indicated that they expect business prospects to decline "somewhat" or "greatly."

[60] Respondents could indicate more than one competitive strategy, so percentages will not add up to 100%.

Table 3.14: Competitive Strategies of Respondents Working in Industrial and Agricultural-derived Processing Applications

Strategic Response to Business Conditions	Number of companies indicating this action	Percentage of companies responding
No change in strategic response	8	6.1
License-out technology	70	53.0
Expand operations	70	53.0
License-in technology	63	47.7
Enter product trials	54	40.9
Refocus R&D activities	70	53.0
Launch a new product	74	56.1
Refocus product development	68	51.5
Increase recruitment efforts for U.S. workers	44	33.3
Outsource production	44	33.3
Expand into foreign markets	48	36.4
Form a joint venture	46	34.8
Merge with other company	11	8.3
Acquire a company	30	22.7
Downsize operations	19	14.4
Recruit employees abroad	17	12.9
Establish facilities abroad	13	9.8
Establish additional R&D collaborations	0	0.0
Other	1	0.8
No response	1	0.8

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

mechanisms for sharing or leveraging technology platforms). Other competitive strategies include outsourcing production (33%) and acquiring another company (23%).

Marine and Terrestrial Microbial

Forty-one respondents (about 5% of the survey population) indicated that marine and terrestrial microbial (MTM) applications were either a primary or secondary focus of their business activities.[61] Of these, 35 (83%) indicated that biotechnology is a central activity of their firm or division.[62] In terms of number of respondents, this application was the smallest; only 15 firms indicated that this application was their primary focus of activity. Twelve MTM companies that selected this category as their primary application have been established since 1990. This high number (80% of such firms) reflects the relatively new application of biotechnologies to microorganisms.

Few primary MTM respondents provided specific information about ownership of their company. However, data from respondents that indicated MTM as a secondary area of biotech activity suggest that Japan, Germany, and Canada are headquarters for owners of several U.S. companies that are active in the area of microbial biotech applications.

As might be expected for companies engaged in marine-based activities, many respondents are located in or adjacent to coastal states; about one-third of respondents are located in California. North Carolina, Maryland, and New Jersey collectively are home to an additional 11 companies.

[61] Analysis presented in this section is based on combined responses for the 41 respondents that indicated this application as either a primary or secondary focus of business activity, unless otherwise noted.

[62] *CTA,* question 7, page 3.

Biotechnology Applications and Activities

In the expanding search for biological organisms that can be used in the prevention, diagnosis, and treatment of diseases or for industrial applications, companies are investigating marine and terrestrial organisms that have adapted to extreme conditions such as high pressure or heat, or total darkness. In the oceans and in extreme conditions on land, these types of "extremeophiles" and other, better-known types of microorganisms are beginning to provide some commercial biotech products.[63] For example, recent studies and research suggest that products derived from diverse microorganisms, including green algae and a painkiller derived from snails, have the potential to be potent weapons in fighting cancer.

Not surprisingly, most MTM respondents (63%) indicated that their research is focused in microbiology, virology, and microbial ecology, followed by extractions, purifications, and separations (61%) (Table 3.15). DNA-based applications were cited by 46% to 59% of MTM respondents, all of which identified MTM biotech applications as a secondary business activity. Microbes also hold promise in diagnostic tests, and 41% of companies indicated research in the area of diagnostics and antibiotics; 37% identified work in synthesis/sequencing of proteins and peptides. Firms also indicated a number of clinical trials under way in these same areas.

Almost one-quarter of MTM respondents reported approved processes related to fermentation, bioprocessing, and biotransformation; 22% cited approved or marketed products in this area. Twenty percent of firms indicated that they have products that are approved, marketed, or in production related to gene probe and DNA markers, and 17% indicated products in DNA sequencing/synthesis/amplification or genetic engineering. Other categories of products included extractions, purifications, and separations (17%); microbiology, virology, and microbial ecology (15%); and diagnostic tests and antibiotics (15%).

In the MTM application area, as in all others, survey respondents reported more pending U.S. patent applications than are currently held in company portfolios (Table 3.16). For firms reporting microbial work as a primary biotech application in 2002, for example, 253 patent applications were pending, compared to 113 active patents. Data indicate that MTM companies also commonly acquire and grant trade secrets to domestic firms. As shown in Table 3.15, survey responses indicated a strong "pipeline" of products and processes in many areas of biotechnology.

MTM Respondents' Economic Characteristics

In 2001, MTM respondents accounted for about 6.5% of all reported biotech employees, 7.8% of reported net sales, 10% of capital expenditures, and 16.3% of reported R&D expenditures (Table 3.16). The dozen firms engaged in microbial activity as their *primary* biotechnology application reported collective negative operating income for their biotech business lines of minus $42.3 million. However, for all MTM respondents, biotech operating income was reported to be about $254 million.

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[63] John, Henkel, "Drugs of the Deep." U.S. Food and Drug Administration. www.fda.gov (viewed April 2, 2002).

Table 3.15: Biotechnology Activities of Respondents Working in Marine and Terrestrial Microbial Applications

	Conduct research on/in (%)	Development, pre-clinical trials, or confined field tests (%)		Clinical trials, or unconfirmed release assessments (%)	Approved, marketed, or in production (%)	
		Product(s)	Process(es)		Product(s)	Process(es)
DNA-based						
Gene probes, DNA markers	49	22	15	7	20	12
Bioinformatics	46	15	12	2	5	0
Genomics, pharmacogenetics	49	15	15	2	7	5
DNA sequencing/synthesis/ amplification, genetic engin.	59	29	22	7	17	10
Biochemistry/Immunology						
Vaccines/immune stimulants	15	10	7	7	0	0
Drug design & delivery	20	5	7	2	0	0
Diagnostic tests, antibiotics	41	20	10	7	15	12
Synthesis/sequencing of proteins and peptides	37	10	10	2	7	5
Cell receptors/signaling, structural biology	22	7	5	5	5	5
Combinatorial chemistry, 3-D molecular modelling	20	10	10	5	7	5
Biomaterials	22	12	10	0	7	5
Microbiology, virology, microbial ecology	63	24	17	17	15	12
Bioprocessing-based						
Culturing/manipulation of cells, tissues, embryos	32	12	7	5	7	2
Extractions, purifications, separations	61	27	24	10	17	20
Fermentation, bioprocessing, biotransformation	56	24	20	10	22	24
Environmental						
Bioleaching, biopulping, biobleaching, biodesulfurization	15	2	2	2	2	2
Bioremediation, biofiltration	17	10	7	5	2	0
Other	5	5	0	0	5	2

41 of the 41 companies in this application category responded to this question.

Cited figures will not in most cases add up to 100%, as the responding companies could list multiple activities.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Table 3.16: Economic and Business Statistics for Respondents Working in Marine and Terrestrial Microbial Applications, 2001

	Companies identifying application as primary		Companies identifying application as primary or secondary		All biotech companies reporting in this survey	
		Cases reporting		*Cases reporting*		*Cases reporting*
Number of businesses in application	**15**		**41**		**1,031**	
Employment (FTEs)						
Entire business	53,946	15	162,875	41	1,134,879	1,030
Biotech activities	419	15	8,556	41	130,305	1,031
Net Sales ($ thousand)						
Entire business	$60,784	12	$44,406,930	35	$566,985,000	976
Biotech activities	$41,428	12	$2,085,801	34	$50,472,720	942
Operating Income ($ thousand)						
Entire business	–$43,338	12	$13,937,910	34	$100,516,300	970
Biotech activities	–$42,288	11	$254,093	33	$9,367,822	938
Capital Expenditures ($ thousand)						
Entire business	$26,570	12	$2,952,617	33	$29,535,620	953
Biotech activities	$26,361	12	$148,046	33	$6,244,325	913
R&D Expenditures ($ thousand)						
Entire business	$70,026	12	$6,792,574	33	$41,590,290	951
Biotech activities	$70,026	12	$491,705	33	$16,440,990	936
Patents						
Total active	113	12	2,092	37	23,992	921
Applications pending	253	15	2,550	37	33,131	928
Exports						
Number of firms exporting	5	11	21	34	388	869

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

In 2001, biotechnology-related R&D accounted for 7.2% of all R&D expenditures reported by MTM respondents. Biotech R&D intensity (as measured by the ratio of R&D expenditures to net sales) was 23.6% for MTM respondents, compared to 15.3% for respondents' entire businesses. However, unlike other biotech applications discussed in this report, capital intensity for biotech business lines was virtually the same as that reported for respondents' entire businesses: 6.6% and 7%, respectively. Biotechnology-related capital expenditures accounted for 5% of MTM companies' total capital expenditures in 2001.

Exports

As noted below, 46.3% of MTM respondents plan to expand into new foreign markets. Currently, almost half of primary MTM companies export, with the most common foreign markets being Canada, France, and Japan and other Asian countries. Some companies reported that exports provide as much as 25% of total firm revenues, although most reported contributions of 5% to 12%.

Government Partnerships and Collaborations

According to survey respondents, venture capital, angel investors, and federal grants are all important sources of funding for MTM applications research; about 46% of responses identified one of these sources. About 55% of respondents indicated in-house or parent firm funding as an important source of funding for biotech R&D. More than half of the companies that provided information about partnerships with government agencies[64] indicated that they had worked with the National Institutes of Health. The Department of Energy was the second most utilized agency.

Future Business Strategies

Although almost 20% of respondents indicated plans to downsize operations, 54% plan to expand operations and 46% plan to expand into foreign markets. In fact, 85% of MTM respondents said they expected near-term business prospects to improve "greatly" or "somewhat," and all but two have developed new near-term competitive strategies.[65] Most of these strategies focus on product and process development (Table 3.17), either by refocusing product development (46%) and R&D (51%), entering product trials (42%), or launching a new product (59%).[66]

As with other survey respondents, technology licensing is an important strategic activity for companies working on microbial biotech applications; 63% indicated that they plan to license their technology to other firms in the near future, while 39% plan to acquire technology through licensing arrangements and 37% plan to form a joint venture (which is often a mechanism for sharing or leveraging technology platforms). Other strategic alliances included outsourcing production (37%) and establishing facilities abroad (20%).

Environmental Remediation and Natural Resource Recovery

Of the 1,031 survey respondents, 41 or 4% indicated that environmental remediation or natural resource recovery (ERNR) was a primary or secondary focus of their biotechnology-related activities.[67] About 70% of respondents (29) indicated that biotechnology was "central" to their firm or division, including seven of the eight largest companies (those with more than 1,000 employees).

Respondents that identified this application as their primary activity reported only 142 employees with biotech responsibilities—the smallest number of any of the survey applica-

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[64] *CTA,* question 29, page 9.

[65] Based on 40 responses to question 33 of the *CTA*. Two companies indicated that they expect business prospects to "decline greatly."

[66] Respondents could indicate more than one competitive strategy so percentages will not add up to 100%.

[67] Although the survey originally provided separate categories for environmental remediation and natural resource recovery, responses have been combined to protect confidentiality of respondents.

tions. Only one large firm (more than 500 employees) reported more than 1,000 employees dedicated to biotechnology activities. However, all ERNR respondents collectively reported 6,116 FTEs with biotech-related responsibilities, almost 5% of the total number reported.

Seventy percent of ERNR respondents were established since 1985, and five predate World War II. No respondents were established in 2001 or 2002, although several firms were acquired. Only one company reported foreign ownership.

Survey data indicate that most ERNR respondents are located in the western United States: 10 in California, two in Colorado and two in Oklahoma, and one each in Arizona, Texas, and Utah. Other states with multiple ERNR firms include New York (three), Ohio (three), North Carolina (two), and Wisconsin (two). Remaining respondent companies are scattered over nine other states.

Table 3.17: Competitive Strategies of Respondents Working in Marine and Terrestrial Microbial Applications

Strategic Response to Business Conditions	Number of companies indicating this action	Percentage of companies responding
No change in strategic response	2	4.9
License-out technology	26	63.4
Expand operations	22	53.7
License-in technology	16	39.0
Enter product trials	17	41.5
Refocus R&D activities	21	51.2
Launch a new product	24	58.5
Refocus product development	19	46.3
Increase recruitment efforts for U.S. workers	13	31.7
Outsource production	15	36.6
Expand into foreign markets	19	46.3
Form a joint venture	15	36.6
Merge with other company	4	9.8
Acquire a company	7	17.1
Downsize operations	8	19.5
Recruit employees abroad	7	17.1
Establish facilities abroad	8	19.5
Establish additional R&D collaborations	0	0.0
Other	0	0.0
No response	1	2.4

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

ERNR Respondents' Biotechnology Applications and Activities

ERNR firms apply life science tools such as genomics, proteomics, and gene shuffling[68] to conventional manufacturing and synthesis processes and inputs, with the goal of discovering new or improved production methods to make industrial raw materials and intermediate and consumer goods. The economic and social impacts of ERNR applications can include greater manufacturing efficiency and lower production costs, less industrial pollution, and resource conservation. Enzyme-catalyzed processes are generally more efficient than chemical processes because input yields are higher and fewer steps are involved (Figure 3.2).

[68] Specific techniques include gene shuffling, bioinformatics, protein engineering, extremeophiles, molecular breeding, high-level gene expression and protein expression, high-throughput screening, fermentation research, creation of DNA libraries, and subsequent assay development. See Appendix C for an explanation of these terms.

Figure 3.2: A Comparison of Traditional Chemistry Processes and Bioprocesses

PRODUCT	TRADITIONAL CHEMISTRY	INDUSTRIAL BIOTECH	ECONOMIC IMPACT	ENVIRONMENTAL IMPACT
Monomer for Nylon	Four synthesis steps	One synthesis step	75% savings on capital equipment	
	Four isolation steps	One isolation step	50% operating cost reduction	
Acrylamide (for water treatment polymers)	<80% process yield	100% process yield	50% capital equipment savings	No toxic metal catalyst
	Low concentration reactor output (high separation and recycle costs)	Product crystallizes during reaction (no separation step)	Lower waste disposal costs	
	Copper metal catalyst			

Source: The Third Wave: Analyst Briefing on Industrial Biotechnology, Conference Proceedings from January 23, 2003. Published by the Biotechnology Industry Organization (BIO), Industrial and Environmental Section.

Much current ERNR research is focused on manipulation of enzymes or enzymatic reactions, but some firms are working to create new industrial products from engineered bacteria or cells. In the immediate future, the most promising applications may be for plastics and fuels,[69] but ERNR firms are also working on applications in optics, materials, and human health. As with other biotechnology applications, identifying the full range of ERNR firms' research and products is complicated by the fact that ERNR applications are developed and adopted within a wide range of industrial sectors, including minerals and fuel, energy, fine and bulk chemicals, textiles, food and feed, and pulp and paper.[70]

Research activities of ERNR respondents were highly concentrated. Of the 40 firms that provided information, almost half (48%) are conducting research in the areas of bioremediation and biofiltration, and 45% cited gene probes and DNA markers. Forty percent of respondents also indicated research activities in three other bioprocessing or microbiology-related areas (Table 3.18).[71] ERNR firms accounted for 2.5% of all biotech R&D reported by survey respondents.

[69] "Climbing the Helical Staircase," *The Economist,* March 29, 2003, p. 18.

[70] See "Biomaterials and Bioprocess," an excerpt from *Biotech 2002,* by G. Steven Burrill (www.burrillandco.com) and "The Application of Biotechnology to Industrial Sustainability," 2001 report by the Organization of Economic Cooperation and Development (www.oecd.org).

[71] Percentages will not add up to 100% because respondents could indicate activity in multiple areas.

Table 3.18: Biotechnology Activities of Respondents Working in Environmental Remediation and Natural Resource Recovery Applications

	Conduct research on/in (%)	Development, pre-clinical trials, or confined field tests (%)		Clinical trials, or unconfirmed release assessments (%)	Approved, marketed, or in production (%)	
		Product(s)	Process(es)		Product(s)	Process(es)
DNA-based						
Gene probes, DNA markers	45	8	5	3	5	3
Bioinformatics	30	10	5	0	3	0
Genomics, pharmacogenetics	23	8	3	0	3	0
DNA sequencing/synthesis/ amplification, genetic engin.	33	10	10	0	10	0
Biochemistry/Immunology						
Vaccines/immune stimulants	10	5	5	5	0	0
Drug design & delivery	8	5	5	5	0	0
Diagnostic tests, antibiotics	25	10	3	0	10	8
Synthesis/sequencing of proteins and peptides	15	8	8	0	0	0
Cell receptors/signaling, structural biology	13	5	5	5	3	3
Combinatorial chemistry, 3-D molecular modelling	10	10	8	5	3	0
Biomaterials	13	8	8	0	0	0
Microbiology, virology, microbial ecology	40	18	13	15	8	3
Bioprocessing-based						
Culturing/manipulation of cells, tissues, embryos	28	5	5	5	5	5
Extractions, purifications, separations	40	13	15	8	8	15
Fermentation, bioprocessing, biotransformation	40	10	15	3	20	18
Environmental						
Bioleaching, biopulping, biobleaching, biodesulfurization	15	0	5	0	3	8
Bioremediation, biofiltration	48	15	18	10	25	25
Other	0	0	0	0	8	0

40 of the 41 companies in this application category responded to this question.

Cited figures will not in most cases add to 100, as the responding companies could list multiple activities.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Although some ERNR products are subject to Environmental Protection Agency (EPA) regulatory approval,[72] the progression from research through approval to marketing and production generally is not as lengthy as for some other biotech applications. Firms did report confined trials or products in development in two categories: bioremediation and biofiltration; and microbiology, virology, and microbial ecology. The relative number of ERNR respondents that reported having approved products or processes was among the highest of any application category. Most products and processes are concentrated in bioremediation and biofiltration; and fermentation, bioprocessing, and biotransformation. About 10% of respondents identified approved products related to diagnostic tests and antibiotics, and DNA sequencing/synthesis/amplification.

Respondents that indicated ERNR applications as their primary biotech activity reported that they have **25** biotechnology-related U.S. patents pending, compared to **69** currently held—less than 1% of survey respondents' reported patent portfolio (Table 3.19). However, all ERNR respondents reported 1,565 patents pending and 1,178 active patents.

ERNR Respondents' Economic Characteristics

Relative to other biotechnology applications, ERNR 2001 financial activity was small, accounting for 2.2% of all survey respondents' reported biotech net sales, 1.4% of reported biotech capital expenditures, and 2.5% of reported biotech R&D (Table 3.19).

Only 27 companies, or about 2.6% of survey respondents, indicated that environmental remediation or natural resource recovery was a primary area of biotechnology application. Twenty-four of these 27 firms reported total biotech net sales of $13.5 million and negative operating income in 2001. However, 41 companies identified ERNR as a primary *or* secondary application focus. This group reported a more robust financial picture: biotech net sales were $1.13 billion, and biotech operating income was positive at $106 million.

Biotech R&D expenditures for the total group of ERNR companies was 21% of their total reported R&D expenditures, and R&D intensity for biotech business lines (calculated as the ratio of biotech R&D expenditures to biotech-related net sales) was about 36%. In contrast, R&D intensity for ERNR respondents' entire businesses was 2.9%. Capital intensity for biotech business lines was 7.6%, similar to the 8.4% for all ERNR businesses.

Exports

More than half of all ERNR respondents (26) reported that they exported in 2001, and several firms reported that exports account for between 15% and 40% of revenues. In addition to the EU, the United Kingdom, Mexico, and Canada, ERNR firms anticipated exporting to Russia, Australia, India, and a number of Asian markets in 2003.

[72] EPA has regulatory authority over microbial products, including pesticides. See Chapter 7 for more information.

Table 3.19: Economic and Business Statistics for Respondents Working in Environmental Remediation and Natural Resource Recovery Applications, 2001

	Companies identifying application as primary		Companies identifying application as primary or secondary		All biotech companies reporting in this survey	
		Cases reporting		*Cases reporting*		*Cases reporting*
Number of businesses in application	**27**		**41**		**1,031**	
Employment (FTEs)						
Entire business	43,842	27	141,462	41	1,134,879	1,030
Biotech activities	142	27	6,116	41	130,305	1,031
Net Sales ($ thousand)						
Entire business	$30,171,160	25	$66,890,870	38	$566,985,000	976
Biotech activities	$13,554	24	$1,130,007	37	$50,472,720	942
Operating Income ($ thousand)						
Entire business	$1,251,689	26	$9,192,160	39	$100,516,300	970
Biotech activities	-$3,340	24	$106,417	37	$9,367,822	938
Capital Expenditures ($ thousand)						
Entire business	$3,299,195	24	$5,645,304	38	$29,535,620	953
Biotech activities	$908	24	$86,533	38	$6,244,325	913
R&D Expenditures ($ thousand)						
Entire business	$99,826	23	$1,948,632	36	$41,590,290	951
Biotech activities	$3,018	23	$415,169	36	$16,440,990	936
Patents						
Total active	69	22	1,178	35	23,992	921
Applications pending	25	20	1,565	33	33,131	928
Exports						
Number of firms exporting	9	23	15	36	388	869

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Government Partnerships and Collaborations

ERNR companies reported that they work with almost every research-oriented agency in the federal government, although they work most often with the U.S. Department of Energy (DOE). It appears that ERNR firms not only avail themselves of grants (especially SBIR grants), but also work with DOE laboratories under technology transfer programs such as CRADA and "Work for Others" arrangements. Respondents identified the Department of Defense and the National Institutes of Health as other federal agencies with which they commonly partner. The U.S. Department of Agriculture (USDA) and the National Science Foundation were also cited frequently.

Analysis of time series data revealed that several respondents moved from reliance on government grants (federal and state) for initial funding to a mix of in-house and private investors

during 2000–02. No company that provided time series data indicated that government funds were a significant source of R&D funding throughout the entire survey period. Sixty percent of ERNR respondents that provided information about the sources of funding for their 2001 R&D biotech budget cited in-house financing and funding from a parent firm as important sources. Only one firm identified venture capital as a funding source, while three indicated that angel investors had contributed some funding.

Future Business Strategies

ERNR respondents are optimistic about the future, with 39% (16) indicating that they expect their competitive business prospects to improve "greatly" or "somewhat" in the next two years.[73] No company indicated that it expects a decline in its business prospects. However, several areas were identified as competitive barriers. Several of the most common concerns for ERNR respondents are related to environmental laws and regulations. Companies cited "antiquated rules and regulations," "unfair U.S. laws," and "government procurement" among the top impediments.

As in most biotechnology applications covered in this report, licensing-out of technology is a popular competitive strategy among ERNR companies responding to the survey, as indicated by more than 46% of firms (Table 3.20). It is also noteworthy that more than 29% of ERNR respondents indicated plans to form a joint venture and almost 27% said they planned to license-in technology, both of which are often ways of gaining access to technological platforms. About 44% of ERNR firms indicated that they plan to launch a new product, while almost 27% said they plan to enter product trials. About a quarter of respondents indicated that they likely would refocus their R&D activities or product development.

For more than half of ERNR respondents, business strategies for the next two years include expanding operations, particularly into foreign markets. About 20% of respondents indicated that they plan to establish a facility abroad, and the same number indicated that they would recruit employees abroad.

Other Applications

Almost 16% of all respondents (160) selected the "other" category when asked to identify their primary and secondary areas of biotechnology activity.[74] In fact, more respondents chose this category than any other except human health, which underscores the difficulty of categorizing biotechnologies. Companies that identified this category as their primary application area (144) included firms that describe themselves as manufacturing biosensors and detection

[73] *CTA*, question 33, page 13.

[74] Analysis presented in this section is based on combined responses for the 160 respondents that indicated this application as either a primary or secondary focus of business activity, unless otherwise noted.

devices and services (10); software and computer systems (15); and hardware, research products for analysis, or other tools (71). Of these 144, 130 indicated that biotechnology is a central activity of their firm or division.

Almost half of all "other" respondents (48%) indicated that they were established prior to 1990. Since 1990, the greatest number of companies (10) was established in 2001. As might be expected, respondents engaged in "other" types of biotechnology applications are found throughout the United States. Thirty-four respondents (21%) are in California, followed by Maryland (14), New Jersey (10), and Texas (9).

Although the majority of respondents are either fully or partially owned by U.S. companies, Japanese and UK companies were cited as owners in several cases. Other foreign owners are in Australia, France, Germany, Sweden, and the Netherlands.

Table 3.20: Competitive Strategies of Respondents Working in Environmental Remediation and Natural Resource Recovery Applications

Strategic Response to Business Conditions	Number of companies indicating this action	Percentage of companies responding
No change in strategic response	5	12.2
License-out technology	19	46.3
Expand operations	21	51.2
License-in technology	11	26.8
Enter product trials	11	26.8
Refocus R&D activities	10	24.4
Launch a new product	18	43.9
Refocus product development	9	22.0
Increase recruitment efforts for U.S. workers	15	36.6
Outsource production	10	24.4
Expand into foreign markets	22	53.7
Form a joint venture	12	29.3
Merge with other company	3	7.3
Acquire a company	6	14.6
Downsize operations	3	7.3
Recruit employees abroad	8	19.5
Establish facilities abroad	8	19.5
Establish additional R&D collaborations	0	0.0
Other	2	4.9
No response	1	2.4

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Biotechnology Applications and Activities

As might be expected, "other" respondents are conducting research in a wide variety of biotechnology areas, with the exception of environmental applications (Table 3.21). The three most commonly identified research categories were extractions, purifications, and separations (28% of respondents); gene probes and DNA markers (27%); and DNA sequencing/synthesis/amplification and genetic engineering (25%). In this respect, firms' activities are similar to those reported by companies working in other application areas such as human or animal health. However, compared to many application areas discussed in this chapter, "other" respondents appear to have relatively few products in the pipeline or approved, marketed, and in production.

In this application area, as in all others, survey respondents reported more pending U.S. patent applications than are currently held in company portfolios—2,010 patent applications were pending for companies that chose this application category as a primary application area, compared

Table 3.21: Biotechnology Activities of Respondents Working in "Other" Applications

	Conduct research on/in (%)	Development, pre-clinical trials, or confined field tests (%)		Clinical trials, or unconfirmed release assessments (%)	Approved, marketed, or in production (%)	
	Product(s)	*Process(es)*		*Product(s)*	*Process(es)*	
DNA-based						
Gene probes, DNA markers	27	9	8	5	10	5
Bioinformatics	19	7	3	1	5	1
Genomics, pharmacogenetics	24	6	4	3	6	5
DNA sequencing/synthesis/ amplification, genetic engin.	25	8	6	3	8	6
Biochemistry/Immunology						
Vaccines/immune stimulants	9	5	2	2	1	1
Drug design & delivery	14	8	3	3	2	1
Diagnostic tests, antibiotics	23	12	8	6	7	6
Synthesis/sequencing of proteins and peptides	20	10	4	3	5	1
Cell receptors/signaling, structural biology	15	3	0	1	3	1
Combinatorial chemistry, 3-D molecular modelling	9	5	1	0	1	0
Biomaterials	11	7	5	2	5	1
Microbiology, virology, microbial ecology	18	10	3	4	5	5
Bioprocessing-based						
Culturing/manipulation of cells, tissues, embryos	21	9	4	3	4	3
Extractions, purifications, separations	28	12	6	3	12	6
Fermentation, bioprocessing, biotransformation	14	7	5	3	7	5
Environmental						
Bioleaching, biopulping, biobleaching, biodesulfurization	0	0	0	0	1	1
Bioremediation, biofiltration	3	1	2	2	1	1
Other	19	6	4	3	9	5

154 of the 160 companies in this application category responded to this question.

Cited figures will not in most cases add up to 100%, as the responding companies could list multiple activities.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry*, August 2002.

to 1,720 active patents. It appears that "other" respondents do not utilize trade secrets to the extent that has been reported by respondents working in some other biotechnology applications.

"Other" Respondents' Economic Characteristics

In 2001, this category of respondents accounted for about 11.4% of all reported biotech employees, 6.8% of reported net sales, 7.4% of capital expenditures, and 6.4% of reported R&D expenditures (Table 3.22). This is one of only two biotechnology applications that reported positive operating income in 2001 ($101.2 million) for primary companies' biotechnology lines of business; total operating income for all "other" companies in 2001 was $15.8 billion.

In 2001, biotechnology-related R&D accounted for 32.9% of all R&D expenditures for companies selecting this category as a primary or secondary focus of their biotechnology activities. R&D intensity for biotech business lines of respondents engaged in "other" biotech applications, as

Table 3.22: Economic and Business Statistics for Respondents Working in "Other" Applications, 2001

	Companies identifying application as primary		Companies identifying application as primary or secondary		All biotech companies reporting in this survey	
		Cases reporting		*Cases reporting*		*Cases reporting*
Number of businesses in application	**144**		**160**		**1,031**	
Employment (FTEs)						
Entire business	29,754	144	125,874	160	1,134,879	1,030
Biotech activities	13,750	144	14,879	160	130,305	1,031
Net Sales ($ thousand)						
Entire business	$11,214,770	139	$75,666,580	154	$566,985,000	976
Biotech activities	$3,284,095	134	$3,426,332	147	$50,472,720	942
Operating Income ($ thousand)						
Entire business	$279,971	137	$15,800,790	151	$100,516,300	970
Biotech activities	$101,216	133	$77,256	147	$9,367,822	938
Capital Expenditures ($ thousand)						
Entire business	$1,296,746	137	$4,638,655	150	$29,535,620	953
Biotech activities	$435,197	122	$462,075	137	$6,244,325	913
R&D Expenditures ($ thousand)						
Entire business	$1,082,478	130	$3,225,983	145	$41,590,290	951
Biotech activities	$829,133	122	$1,060,056	138	$16,440,990	936
Patents						
Total active	1,720	129	2,484	144	23,992	921
Applications pending	2,010	132	2,539	148	33,131	928
Exports						
Number of firms exporting	94	132	100	146	388	869

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

measured by a ratio of R&D expenditures to net sales, was 30.9%, in contrast to 4.3% for their entire businesses. Similarly, capital intensity was greater for biotech business lines than for respondents' total businesses—13.5% compared to 6.1%. Capital expenditures in biotechnology-related business lines accounted for about 10% of "other" companies' total capital expenditures.

According to survey respondents that indicated this as a primary area of biotechnology-related activity, venture capital funding and angel investors were an important part of their R&D funding stream in 2001, exceeding even federal loans and grants in terms of frequency (e.g., number of firms that indicated using them). Nevertheless, as with all other types of biotechnology applications, in-house revenues and parent firm funding were cited almost 50% more often than all other sources combined.

Exports

About 28% of "other" respondents plan to expand into new foreign markets, and about 71% export. No single country or region was identified as the most important market, but Canada, Mexico, and the EU are clearly important trading partners for companies that work in "other" biotechnology applications.

Future Business Strategies

Although about 8% of respondents indicated plans to downsize operations, 53% plan to expand operations, and 54% have plans to launch a new product, almost half that number (21%) indicated that they expect to enter product trials (Table 3.23). Over one-third of firms noted plans to refocus R&D (34%) and product development (39%). About 78% indicated that they view near-term business prospects as likely to improve "greatly" or "somewhat" and all but 18 have developed new near-term competitive strategies.[75]

As with other types of biotechnology companies, technology licensing is an important strategic activity for these companies, with nearly equal numbers citing intentions to license-in (39%) and license-out (38%) technologies. Like most other respondents, about one-third of companies engaged in "other" biotechnology applications are developing recruitment strategies for U.S. workers; only about 8% of responses indicated strategies to recruit employees abroad.

Respondents with Defense Contracts

The defense sector is a customer to many companies involved in the field of biotechnology, and national defense agencies are increasingly interested in biotechnology's capabilities.[76] At least 105 of the 1,031 companies that participated in the *CTA* survey reported that they

[75] Based on 132 responses to question 33 of the *CTA*. Five companies indicated that they expect business prospects to decline "somewhat" or "greatly."

[76] See, for example, *Opportunities in Biotechnology for Future Army Applications,* National Research Council, 2001.

have held a contract with the Department of Defense (DoD) or other defense organizations. For the most part, survey results do not reveal dramatically different behavior on the part of companies that have held defense contracts and those that do not perform defense work as part of either their biotechnology activities or other business operations.

Of the 1,031 companies that responded to the survey, 929 provided information on whether they have held defense contracts in the last five years.[77] Eleven percent of these enterprises (105) have held defense contracts (not necessarily linked to biotechnology) as a prime contractor or subcontractor. Approximately 72% of these firms (76) had active defense contracts of some kind at the time the survey was distributed to them in 2002.

Biotechnology Applications and Activities of Respondents with Defense Contracts

The business focus of respondents that have held defense contracts of any kind between 1997 and 2001 is similar to that of the entire survey population. Human health applications (therapeutics, diagnostics, and prevention) were reported to be the primary application focus by 72% of all respondents, compared to 75% of respondents (79) that reported holding defense contracts during this period. Nineteen percent of companies that accept defense work ranked animal health as a primary or secondary area of interest, compared to 14% for all respondents. The application of biotechnology for production of specialty chemicals, enhancing production of agriculture-based materials, and food processing is also a lead area of interest. Nearly 17% of companies performing defense work cited this category as a primary or secondary area of interest, compared to almost 13% of respondents that have not held defense-related contracts.

Table 3.23: Competitive Strategies of Respondents Working in "Other" Applications

Strategic Response to Business Conditions	Number of companies indicating this action	Percentage of companies responding
No change in strategic response	18	11.3
License-out technology	61	38.1
Expand operations	85	53.1
License-in technology	62	38.8
Enter product trials	33	20.6
Refocus R&D activities	55	34.4
Launch a new product	87	54.4
Refocus product development	62	38.8
Increase recruitment efforts for U.S. workers	49	30.6
Outsource production	26	16.3
Expand into foreign markets	45	28.1
Form a joint venture	27	16.9
Merge with other company	21	13.1
Acquire a company	22	13.8
Downsize operations	13	8.1
Recruit employees abroad	12	7.5
Establish facilities abroad	9	5.6
Establish additional R&D collaborations	0	0.0
Other	3	1.9
No response	1	0.6

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

[77] For the purposes of this chapter, companies engaged in defense work were identified on the basis of whether or not they answered "Yes" to question 39 of the survey. It asked businesses if they had held a defense contract, as a prime contractor or subcontractor, within the last five years. The term "last five years" is interpreted to mean either calendar years or business years 1997 through 2001.

Business Practices

Companies that have held or currently hold defense contracts were asked specific questions about their business practices in working with defense contractors and government agencies. Respondents appear to engage in a considerable amount of custom contract work, as well as filling contracts for commercial products. Responding to a question about whether their products were sold to DOD as commercial items, almost 41% of 101 companies responded affirmatively.[78] Another 60 businesses that have held defense contracts, however, stated that they did not sell their products to DOD as commercial products.

It appears that most of the companies that take on defense work meet their contract obligations using the same workers, equipment, and physical plant that are employed for commercial contracts. Fifty-nine of the 105 companies that acknowledged having defense contracts in the last five years responded to a question on whether value-added inputs for defense and commercial products could be attributed to a common infrastructure (Table 3.24). Of these 59 companies, 54 reported using shared infrastructure.

As a matter of business practice, many, if not most, companies that have held defense contracts do not require longer lead times for defense contracts than are normally set for orders of commercial goods and services. While just 49 companies responded to the questions about their practices, 42 of the 49 said their lead times for commercial and defense contracts were the same.

Survey results also suggest that there is some level of sophistication among companies that engage in biotechnology and take on defense contracts. Of the 105 contractors that have held defense contracts in the last five years, 67 companies report having registered with the Central Contract Registration[79] office. This organization is a central repository of all companies and agencies wanting to do business with DOD.

Economic Characteristics of Respondents with Defense Contracts

Respondents with defense contracts accounted for about 19.6% of all reported biotech employees. Comparing biotech lines of business, this group of firms accounted for 16.2% of reported net sales, 13% of capital expenditures, and 17.6% of reported R&D expenditures (Table 3.25).

An examination of R&D spending as a percenage of net sales across all business units (biotech and nonbiotech) of all survey respondents shows little difference in the percent of R&D spending on average for survey participants that handle defense contracts and those that do not. R&D intensity (R&D expenditures as a percentage of net sales) across all business operations was 8.2% for the 78 respondents that have held defense contracts, compared to 9.5% for firms

[78] See survey question 40.

[79] As of June 1, 1998, all companies and agencies must be registered and validated with the Central Contract Registration office to qualify to enter into any contract, basic agreement, basic ordering agreement, or blanket purchase agreement. See http://www.ccr.dlis.dla.mil/ccr/scripts/index.html (viewed July 2003).

Table 3.24: Business Practices of Respondents with Defense Contract Experience

Questions	Y	N
Q.39—Firms that held defense contracts in the last five years	105	824
Q.40—Does your firm sell this product to DOD as a commercial or nondevelopmental item?	41	60
Q.41—Firms that currently have a defense contract	76	28
Q.43—Are the value-added inputs of defense and commercial products attributed to the same facilities, employees, and equipment?	54	5
Q.44—Is production lead time the same as that quoted to commercial customers?	42	7
Q.45—Is your business registered in the Central Contract Registration?	67	21

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002. Only companies that responded "yes" in question 39 were included for questions 40, 41, 43, 44, and 45.

Table 3.25: Economic and Business Statistics for Respondents with Defense Contracts, 2001

	Companies with business relations with DOD or other defense organizations		All biotech companies reporting in this survey	
		Cases reporting		*Cases reporting*
Number of businesses in application	**105**		**1,031**	
Employment (FTEs)				
Entire business	536,659	105	1,134,879	1,030
Biotech activities	25,507	105	130,305	1,031
Net Sales ($ thousand)				
Entire business	$280,460,200	102	$566,985,000	976
Biotech activities	$8,201,758	105	$50,472,720	942
Operating Income ($ thousand)				
Entire business	$51,464,100	102	$100,516,300	970
Biotech activities	$1,462,108	100	$9,367,822	938
Capital Expenditures ($ thousand)				
Entire business	$11,309,740	95	$29,535,620	953
Biotech activities	$812,739	93	$6,244,325	913
R&D Expenditures ($ thousand)				
Entire business	$11,364,520	100	$41,590,290	951
Biotech activities	$2,896,304	99	$16,440,990	936
Patents				
Total active	5,209	98	23,992	921
Applications pending	5,761	100	33,131	928
Exports				
Number of firms exporting	47	95	388	869

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

that do not handle defense contracts. R&D intensity for biotech business lines was 32% for companies that have held defense contracts, compared to 27% for those that did not.

Capital expenditures are a major cost for companies that participate in the biotechnology industry, including those that perform defense work. Data provided in 839 surveys show combined outlays for biotechnology-related activities of about $6.2 billion for 2001—of which approximately $812 million is attributed to 91 companies that have held defense contracts. However, capital intensity is similar for both groups: 9.6% for respondents with defense contracts and 11.8% for all others.

Outlook and Future Business Strategies

For the most part, respondents that hold defense contracts were optimistic about the future, with 81.9% indicating that they expect near-term business prospects to improve "greatly" or "somewhat." Almost half (48.6%) reported they would expand operations, launch a new product (51.4%), and/or enter product trials (39.0%), while only 11.4% said they expected to downsize. Almost a quarter of all firms (23.8%) reported that they planned to expand into foreign markets, and 10.5% said they would establish facilities abroad. This is an optimistic view, given that 49 of the 105 firms in this category had little or no operating income. Respondents also described their plans for workforce recruitment (see Chapter 6).

Of particular interest are data indicating that a significant number of companies that have held defense contracts in the last five years plan to increase their ability to conduct research and produce products in more stringently regulated laboratory environments.

Currently, a total of 50 companies that have held defense contracts (about 48%) reported having Level-2 biosafety facilities, compared to about 27% of firms that had not held such contracts. Typically, this biosafety level imposes control procedures for aerosols or splashes of infectious biological material and pathogenic agents through the use of physical containment and controlled working conditions, procedures, and sanitation practices.[80] Across all biotechnology-related applications, the use of Level-2 facilities is relatively common.

In the case of companies that perform defense work, only 13 of 61 respondents (21%)[81] reported having Level-3 facilities, compared to 37 (3.6%) for other firms. Level-3 safety requirements are imposed on clinical, diagnostic, production, research, and teaching activities that involve pathogenic or lethal agents. In addition to standard laboratory practice requirements and controls stipulated under Level-2, protocols for Level-3 activities require implementation of architectural standards controlling access and airflow, stricter hazardous material handling and decontamination procedures, and systematic monitoring of the workforce in the facility.

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[80] See Centers for Disease Control standards at http://www.cdc.gov/od/ohs/biosfty/bmbl4/bmbl4s3.htm.

[81] *CTA*, question 10, page 3.

Level-4 safety standards require a separate building or a completely closed off area of a building. These facilities must be equipped with Class III safety cabinets or Class III safety suits fitted with positive pressure suits and independent life support systems. In addition, architectural and operating procedures that are significantly more stringent than those imposed for Level-3 facilities are imposed. No company reported operating a Level-4 facility.

Whether or not they perform defense work, it is routine for businesses in the biotechnology field to seek to advance the science and to push product development goals. This competitive drive is certainly one reason behind the decisions of businesses to build new Level-3, and perhaps Level-4, research and/or production facilities. In some quarters of the industry, the need for more highly certified research facilities may have arisen after the anthrax attacks that occurred in the fall of 2001. There is clearly an increased interest in industry and the government in developing antidotes and countermeasures against pathogenic organisms and toxic chemicals that terrorists could release in populated environments.

At least 16% (17 of the 105) of biotechnology companies that have held defense contracts in recent years disclosed that they plan to construct new Level-3 or Level-4 facilities in the next three years. Fifteen of these new facilities are to be built by small and medium-sized companies. Only 4%, or 39, of 736 firms that did not hold defense contracts between 1997 and 2001 reported that they plan to build Level-3 or Level-4 facilities in the next three years; 35 of the units would be constructed by small or medium-sized companies.[82]

[82] What is not clear in the responses of both firms that undertake defense work and those that do not, is precisely how many Level-3 facilities and/or Level-4 units companies intend to build. Question 11 did not require businesses to provide specific information on the number or type of each kind of facility.

Chapter 4
Financial and Economic Performance

New technologies have the potential to contribute to national economic growth as they transform industries by creating new products, improving production processes, and accelerating the pace of innovation. Survey data demonstrate that the use of biotechnology in industry is increasingly widespread and that biotechnology companies are of growing importance to the U.S. economy. These contributions are reflected in increasing net sales of biotechnology goods and services and greater capital expenditure growth and intensity attributed to the biotechnology-related business lines compared to respondents' entire businesses.

Net Sales

In 2001, survey respondents' net sales of biotechnology products and services were $50.5 billion.83 This represented about 9% of respondents' entire business net sales, which totaled $567 billion (Table 4.1). Twenty-six percent of respondents (268) reported zero net sales in 2001.

In 2001, the value added[84] of respondents' biotechnology business lines was *at least*[85] $33.5 billion, or 0.33% of the $10 trillion U.S. gross domestic product (GDP) in 2001 (current dollars). The value-added estimate for respondents' entire business activity was $272.8 billion, and thus accounted for *at least* 2.7% of U.S. GDP in 2001. While net sales of the respondents' biotechnology activities were about 9% of the entire business, the value added of the respondents' biotechnology activities was proportionally greater, representing 12% of the entire business.

In 2001 and 2002, growth of biotechnology net sales[86] outpaced that of sales for the overall business operations of respondents (Table 4.1). For these two years, growth rates for biotechnology net sales averaged a little over 10.3% per year, whereas overall business net sales rose at an average annual rate of about 5.9%. Biotech business lines of respondents were comparatively resilient during the economic downturn of 2001; net sales growth for the biotechnology segment of responding companies was 10.5%, while that for the overall business of these companies was only 2.3%.

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[83] Analysis focuses on 2001 because this year provides the most complete response rate for financial data (e.g., all respondents were asked to provide data for this year, including firms with 50 employees or fewer).

[84] Value added is an industry's net addition to gross domestic product. The term "net" signifies that purchases from other industries have been subtracted out of the gross output of the industry to eliminate double-counting. Here, value added has been estimated as net sales less cost of goods sold.

[85] This calculation significantly understates the value added, as it excludes not only purchased inputs but also in-house production costs, including labor. Given that total biotechnology net sales were $50.5 billion, the upper bound would be less than 0.5% of GDP in 2001.

[86] Share-weighted growth rate calculations are mostly based on firms with over 50 employees, because firms with 50 or fewer employees were asked to provide financial information only for 2001. These firms constituted 59% of entire survey respondents, although some firms in this size category did provide financial data for two or more consecutive years.

Table 4.1: Net Sales, Costs of Goods Sold, Selling, General and Administrative Expenses, and Operating Income, 2001

	Total	Average	Number of Respondents	Biotechnology as % of Entire Business	Percent Growth 2000 to 2001	Percent Growth 2001 to 2002	Percent Growth 2002 to 2003
	($000)	($000)					
Entire Business							
Net Sales	566,985,036	607,701	933		2.3	9.5	6.2
COGS	294,233,119	324,045	908		13.4	15.1	5.7
SGAE	163,099,120	176,514	924		–6.2	1.5	6.0
Operating Income	100,516,296	107,966	931		–3.9	7.0	9.4
Biotechnology Business							
Net Sales	50,472,718	56,143	899	8.9	10.5	10.1	16.2
COGS	16,997,349	19,381	877	5.8	15.0	11.5	13.2
SGAE	22,514,823	25,355	888	13.8	11.7	8.5	10.6
Operating Income	9,367,822	10,420	899	9.3	1.1	14.1	39.9

Note: Analysis is based on the subset of respondents that provided useable data. Firms that responded with "0" for all financial questions generally were not included in calculating averages. Totals and growth rates are not affected, but averages may differ from those presented in Chapter 3 as a result.

COGS = cost of goods sold; SGAE = selling, general, and administrative expenses.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Cost of Goods Sold and Sales, General, and Administrative Expenses

The cost of goods sold (COGS) for the biotechnology activities of responding firms accounted for a small percentage of the COGS for their entire businesses. COGS and selling, general, and administrative expenses (SGAE) for the entire businesses of the respondents were $294 billion and $163 billion in 2001, compared to $17 billion and $23 billion for the biotechnology business segments. While the biotechnology business segments of responding firms accounted for only 5.8% of the COGS for the entire business, it represented 13.8% of SGAE. The biotechnology business segment had proportionally higher SGAE and lower cost of goods sold because many of the firms had zero net sales and therefore did not incur the costs for producing goods. Average growth in COGS in 2001 and 2002 combined (based on firms that provided sufficient data) was similar for both the entire and biotechnology business lines of respondents, averaging 14.3% and 13.3%, respectively. During the same time, average growth of SGAE was minus 2.4% for the entire businesses, but averaged 10.1% annually for biotech business lines.

Operating Income

In 2001, the total operating income[87] of respondents approached $101 billion; of this, 9.3% or $9.4 billion represented operating income from the biotechnology business lines. Although 56% of respondents reported either no operating income or negative operating income for their biotechnology business lines in 2001, this does not necessarily mean that these companies were failing. Many smaller firms rely on income from other sources, such as sales of other goods, licensing revenues and funding from capital, federal grants, and angel investments (see Chapters 2 and 3).

While growth in operating income related to the biotechnology activities of respondents was a slightly positive 1.1% in the 2001 recession year, it declined 3.9% for their entire business operations. In 2002, operating income of the biotechnology business segment of firms expanded at twice the rate of growth for the entire businesses of reporting firms; the respective growth rates were 14.1% and 7%.

Survey respondents were generally optimistic about the future. They estimated that growth in total net sales and in operating income, especially related to their biotechnology businesses, would continue to rise substantially in 2003,[88] at 16.2% and almost 40%, respectively.

Costs and Operating Income Performance

An analysis of costs and operating income as a percentage of net sales indicates that the biotechnology business segments of responding companies are performing well financially, keeping up with their entire business operations. These measures are indicators of business performance and financial health. Table 4.2 displays the percentage of net sales attributed to costs and operating income for respondents' entire businesses and for their biotechnology business lines.

The biotechnology businesses of responding firms had lower costs per dollar of net sales than their entire business—34% versus 52% of net sales were apportioned to costs of goods sold. The percentage of net sales not devoted to COGS, therefore, was 66% for the biotechnology business lines and 48% for the entire business. However, biotechnology business lines did not fare as well in terms of SGAE per dollar of net sales: 45% versus 29%. The reason for this difference is that many of the biotechnology business segments of respondents are generating few or no sales and not incurring cost of goods sold, but do incur business expenses. As a result, operating income as a percentage of net sales for the entire and biotechnology business lines were about equal, 18% and 19%, respectively.

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[87] Operating income is net sales minus COGS and SGAE. It differs from a value-added measure because it excludes SGAE, while our added estimate does not.

[88] Respondents were asked to estimate their financial outlook for 2003. Those that responded to this question indicated a positive outlook.

Labor Productivity

Labor productivity for respondents' biotechnology business segments appears to be relatively high compared to most industries, although survey data were limited to a subset of reporting firms. In 2001, the labor productivity level for companies responding to the *CTA* survey was between $257,000 and $388,000 per FTE or employee[89] for respondents' biotechnology lines of business.[90] Despite flat growth for reporting firms of 0.01% between 2000 and 2001, productivity growth increased significantly in 2002, rising at an estimated rate of 8.6% (Table 4.3) for the biotechnology business operations of the one-third of all respondents that provided data.[91] This robust growth rate surpassed even the 4.8% growth rate for the entire U.S. nonfarm business economy during the latter period.

Table 4.2: Costs and Operating Income as Percentage of Net Sales, 2001

	Cost of Goods Sold (%)	Selling, General, and Administrative Expenses (%)	Operating Income (%)
Entire Business	52	29	18
Biotechnology Business	34	45	19

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry*, August 2002.

Table 4.3: Labor Productivity Growth for Respondents' Biotechnology Business Lines

	2000–2001	2001–2002
Percent Growth	0.01	8.68
Number of Respondents	303	345

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry*, August 2002.

[89] The lower bound measure is based on an estimate of value added, or the ratio of net sales minus the cost of goods sold per FTE in 2001. The upper bound is based on total net sales.

[90] For the entire business of respondents, the range of labor productivity for biotechnology business lines was larger than for their entire business, ranging from $232,000 to $491,000.

[91] The share-weighted productivity growth rate was based on a panel of about one-third of survey respondents that provided data on both the biotechnology net sales and employment questions for at least two concurrent years between 2000 and 2002. Additionally, as for all of the share-weighted growth calculations, firms that had fewer than 50 employees were required to provide financial data only for 2001. Therefore, the productivity analysis is largely based on data provided by larger firms. Furthermore, the growth rate was calculated using the labor productivity ratio of net sales minus the cost of goods sold or value added per FTE. See Appendix B.

Capital Expenditures

In 2001, respondents' total expenditures for plant and facilities, machinery and equipment, and total capital were $6.1 billion, $10.7 billion, and $29.5 billion,[92] respectively. Capital expenditures in the biotechnology segment of these businesses represented a substantial amount of respondents' entire business capital expenditures for that year. In 2001, biotechnology-related spending for plant and facilities, machinery and equipment, and total capital were $2.7 billion (44% of respondents' total capital expenditures), $3.3 billion (31%), and $6.2 billion (21%), respectively (Table 4.4). Biotechnology business activities accounted for 0.56% of total U.S. capital expenditures, while respondents' entire business capital expenditures accounted for 2.7% of total U.S. capital expenditures. Capital expenditures for all U.S. industries totaled $1,110 billion in 2001.[93]

While capital expenditure growth related to respondents' biotechnology business segments slowed from 22.8% in 2001 to 12.3% in 2002, it remained higher than that for their entire business and for the entire U.S. economy (Table 4.4). In comparison, annual growth in capital expenditures of the entire business of these firms averaged 9.0% in 2001 and 2002. For the entire U.S.

Table 4.4: Capital Expenditures by Entire and Biotechnology Business Lines, 2001

	Total	Average	Number of Respondents	Biotechnology as % of Entire Business	Percent Growth 2000 to 2001	Percent Growth 2001 to 2002	Percent Growth 2002 to 2003
	($000)	($000)					
Entire Business							
Total Capital	29,535,522	31,025	952		9.2	8.8	7.4
Plant and Facilities	6,091,733	6,922	880		13.6	11.2	22.5
Machinery and Equipment	10,676,722	11,969	892		3.9	12.0	3.9
Biotechnology Business							
Total Capital	6,244,225	6,847	912	21.1	22.8	12.3	10.3
Plant and Facilities	2,661,945	3,113	855	43.7	32.3	6.4	19.0
Machinery and Equipment	3,259,316	3,742	871	30.5	11.9	14.8	–2.1

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

[92] While total capital expenditures should equal expenditures on plant and facilities plus machinery and equipment, total capital expenditures reported here are greater than expenditures on plant and facilities and machinery and equipment combined, primarily because many respondents provided information only on total capital expenditures and did not divide that total to plant and facilities into machinery and equipment.

[93] Capital expenditures are in current dollars.

economy, growth in capital expenditures declined 4.4% in 2001. The high levels of capital spending in biotechnology-related businesses reflect, in part, the unprecedented financing year that biotechnology companies experienced in 2000. In that year, biotechnology companies received more funds from venture capital and initial public offerings (IPOs) than in any previous year.[94]

In 2001 and 2002, respondents' capital expenditure growth averaged 12.4% for plant and facilities and 7.9% for machinery and equipment. Average growth in capital expenditures related to plant and facilities and machinery and equipment was much larger for the biotechnology business segments of responding firms—19.3% and 13.3% in 2001 and 2002, respectively. While respondents expected substantial growth in plant and facilities expenditures for their entire and biotechnology businesses in 2003, they expected a slowdown in machinery and equipment expenditures.

Capital Investment Intensity

Respondents' biotechnology business lines were found to be more capital-intensive than their entire businesses, as calculated by total capital expenditures per dollar of total net sales.[95] In 2001 capital expenditures represented 12.4% of total net sales for respondents' biotech business lines, compared with 5.2% for their entire businesses (Table 4.5).

Table 4.5: Capital Expenditure Intensity Measures, 2001

	Capital Expenditures/Net Sales (%)	Capital Expenditures/FTEs
Entire Business	5.2	$26,000
Biotechnology Business	12.4	$48,000

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Another measure that illustrates the capital investment intensity of the biotechnology segments of these companies is capital expenditures per employee. This measure also shows that respondents' biotechnology business segments were more capital-intensive than their entire businesses. Biotechnology-related capital expenditures per employee were $48,000 in 2001, compared to $26,000 per employee for the entire business. Both of these capital-investment intensity indicators show that respondents were investing about 1.85 times as much in biotechnology capital per employee and per dollar of net sales than for their entire business operations.

[94] An industry analysis and discussion of biotechnology financing can be found in Ernst & Young, "Focus on Fundamentals: The Biotechnology Report," 15th Annual Review, October 2001.

[95] Capital intensity measures were based on *totals* for capital expenditures, net sales and employment for 2001.

Chapter 5
Research and Development Expenditures

Survey respondents reported $16.4 billion in biotechnology-related R&D in 2001. This investment represents 9.8% of the total U.S. industry R&D investment of $168.4 billion in that year—a not insignificant contribution.[96] Despite the fact that many biotech companies have little sales revenue, this level of R&D spending compares favorably with the R&D expenditures of many industry sectors.[97] For example, respondents' share of U.S. industry R&D exceeded that of the aerospace, machinery, or chemical industries, which ranged between 3% and 5.4% in 2000. It was nearly half the 19.8% share of national industry R&D accounted for by the medical substances and devices industry.

More than 82% of firms that reported conducting biotech R&D conduct biotech R&D exclusively. For these 884 survey respondents, about 45.4% or $16.4 billion of their total $36.2 billion R&D investment was directed toward biotechnology-related activities in 2001 (Table 5.1).[98]

Firm Size Category Highlights

Data indicate that as firm size decreases, the share of total R&D investment that is devoted to biotechnology-related projects generally increases. For firms that reported their R&D expenditures, firms with 51 to 500 employees had the highest total R&D investment, at $4.6 billion, and claimed the greatest share of both numbers of biotech scientists and engineers (10,800) and biotech U.S. patents held (7,675). The median for the 283 firms in this size category was

Table 5.1: Biotech Share of Total R&D by Firm Size Category, 2001

Firm size category by number of employees	Percentage of total category R&D that is biotech R&D	Percentage of firms that conduct biotech R&D exclusively
>15,000	22.7	17.6
2,501–15,000	37.0	17.2
501–2,500	75.7	55.1
51–500	91.8	81.6
11–50	98.3	93.0
1–10	101.9	88.9
Total	45.4	82.3

*The aggregate basis percentage for the 1–10 employee category company is somewhat exaggerated because not all firms in this category reported their total R&D expenditures.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

[96] National Science Foundation, Division of Science Resources Statistics, *National Patterns of R&D Resources: 2002 Data Update (current to October 2002)* (NSF 03-313): Table 1A. (Arlington, Va., March 2003). See http://www.nsf.gov/sbe/srs/nsf03313/start.htm (viewed June 2003).

[97] This analysis is based on 2000 data published by the National Science Foundation. See Office of Technology Policy, U.S. Department of Commerce, *U.S. Corporate R&D Investment, 1994–2000 Final Estimates* (Washington, D.C., November 2002), http://www.technology.gov/reports.htm (viewed June 2003).

[98] Since surveyed companies with 50 employees or fewer were only required to provide 2001 data, analysis centers on R&D activity in that year.

$10.2 million in R&D expenditures, 25 biotech scientists and engineers, and 15 biotech U.S. patents held (Table 5.2).[99]

Respondents with 501 to 2,500 employees were among the most active in terms of R&D. The combined biotech R&D expenditures of the 49 respondents in this category were the third highest of the six firm size categories. Nevertheless, median R&D expenses were the highest ($37.1 million) of any category by a substantial margin, as were the median capital investments, net sales, full-time biotech employees, scientists and engineers, and number of patents per company. Other highlights of this group include the following:

- A higher percentage of R&D directed toward development than is the case with smaller reporting firms. On a median basis, 60.8% of expenditures are directed toward development; the next highest development median is 39% for firms in the 2,501 to 15,000 firm size category. It is also substantially more than the median for firms in the two largest firm size categories.

- By far the highest number of companies reporting positive sales: 86%, compared to only 67% for all biotech R&D companies.

- The lowest ratio of biotech scientists and engineers to total biotech employees, but the highest ratio of biotech R&D investment per scientist/engineer (Table 5.3).

These data suggest that unlike many biotech companies that are principally focused on research and the development of future products, mid-sized firms of 501 to 2,500 employees have moved from a principal focus on R&D to product manufacture.

Research vs. Development

Of the 884 survey companies that reported R&D investment in 2001, 680 provided disaggregated data on separate expenditures for research and for development (Table 5.4). These firms invested $5.6 billion on research and $6.8 billion on development, a distribution of about 45% and 55%. While this distribution is weighted more toward development (as is generally the case in industry), respondents' emphasis on research is considerably greater than the 29.1%

[99] The median is the number in the middle of a set of numbers; that is, half the numbers have values that are equal or greater than the number, and half have values that are equal or less. If there is an even number of numbers in the set, then the median is calculated as the average of the two numbers in the middle. The median is less sensitive to extreme numbers (such as those of some very large survey respondents) than the mean (average). The median is particularly useful in the analysis of an industry that includes many small growing firms (especially of a research nature), whose activity can be overshadowed by a few very large firms that produce products. Historically, the character, direction, and growth of emerging industries are usually set by new small firms that generate disproportionately large contributions to technological innovation.

Table 5.2: Financial and Patents Overview for 884 Survey Firms Reporting R&D Performance, 2001 ($ thousands)

Firm size category by number of employees	Number of companies	Aggregate totals		
		Total non-biotech and biotech activity	Biotech activity only	
		R&D investment	R&D investment	U.S. biotech patents held
>15,000	18	15,353,687	3,478,368	2,432
2,501–15,000	29	10,097,255	3,735,319	4,285
501–2,500	49	4,704,300	3,563,309	5,968
51–500	283	5,025,119	4,612,391	7,675
11–50	299	904,083	888,490	2,431
1–10	206	160,243	163,329	590
Total	884	36,244,688	16,441,206	23,381
		Median company activity per category		
>15,000	18	745,000	20,736	45
2,501–15,000	29	139,940	5,600	30
501–2,500	49	53,355	37,144	63
51–500	283	11,655	10,233	15
11–50	299	1,664	1,600	3
1–10	206	213	205	1
Total	884	2,584	2,000	5

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Table 5.3: Employment Overview for 884 Survey Firms Reporting R&D Performance, 2001 ($ thousands)

Firm size category by number of employees	Aggregate basis				Median company basis			
	Total non-biotech & biotech full-time employees	Biotech activity only			Total non-biotech & biotech full-time employees	Biotech activity only		
		Full-time employees	Biotech scientists & engineers*	Ratio of S&Es to full-time employees		Full-time employees	Biotech scientists & engineers*	Ratio of S&Es to full-time employees
>15,000	752,936	20,578	8,208	39.9%	38,250	237	51	21.5%
2,501–15,000	184,062	36,652	6,487	17.7%	5,043	155	41	26.5%
501–2,500	59,328	29,544	5,550	18.8%	1,084	535	111	20.7%
51–500	47,101	29,797	10,800	36.2%	120	78	25	32.1%
11–50	7,740	5,888	2,589	44.0%	23	17	7	41.2%
1–10	1,160	856	623	72.8%	6	4	3	75.0%
Total	1,052,327	123,313	34,257	27.8%	37	22	9	40.9%

*Includes contract employees.

S&Es = scientists and engineers.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Table 5.4: Disaggregated Data for Biotechnology Research and Development Expenditures, 2001

Firm size category by number of employees	Research investment ($ thousands)	Development investment ($ thousands)	Percentage distribution*			
			Aggregate basis		Median company basis†	
			Research	Development	Research	Development
>15,000	1,117,096	2,306,672	32.6	67.4	62.9	37.1
2,501–15,000	958,587	1,034,476	48.1	51.9	60.9	39.1
501–2,500	915,794	1,460,933	38.5	61.5	39.2	60.8
51–500	2,100,115	1,705,587	55.2	44.8	61.0	39.0
11–50	468,614	258,593	64.4	35.6	80.9	19.1
1–10	85,908	52,539	62.1	37.9	96.7	3.3
Total	5,646,114	6,818,799	45.3	54.7	73.8	26.2

*Percentages are based on only the combined R&D of the 680 firms that reported biotech research and development separately. Therefore, totals will differ from others provided in this chapter.

† See footnote 99.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

apportioned by U.S. industry generally in 2000.[100] Moreover, the median biotech research expenditure of 73.8% suggests that most biotech firms are focused on early-stage innovation rather than product development. Just over 60% of respondents spent more on research than development, while 6.6% invested equally between the two activities.

R&D Intensity

Based on total reported data from all survey R&D firms, respondents' R&D intensity for their biotech business lines (the ratio of biotech R&D investment to biotech net sales) was 33.4% in 2001 (Table 5.5). This level was substantially above the national average of 4.3% for corporate spending on R&D in 2000, and nearly three times higher than R&D intensity in the medical substances and devices sector, the leading U.S. industry sector for intensity of R&D investment.[101] This extraordinarily high ratio can be attributed, in part, to the fact that nearly one-third of the 884 companies reporting R&D have yet to develop marketable products and are without significant sales.

[100] Most recent data available. National Science Board, *Science and Engineering Indicators 2002, Appendix Tables* (Washington, D.C., January 2002).

[101] This analysis is based on 2000 data published by the National Science Foundation. See Office of Technology Policy, U.S. Department of Commerce, *U.S. Corporate R&D Investment, 1994–2000 Final Estimates* (Washington, D.C., November 2002), http://www.technology.gov/reports.htm (viewed June 14, 2003).

Table 5.5: Measures of Biotech R&D Intensity, 2001 (full dollar amounts)

Firm size category by number of employees	Aggregate basis				Median company basis			
	Biotech R&D investment as a percentage of biotech sales	Biotech R&D investment per biotech employee	Biotech R&D investment per biotech scientists & engineers	Biotech R&D investment per number of current patents held*	Biotech R&D investment as a percentage of biotech sales	Biotech R&D investment per biotech employee	Biotech R&D investment per biotech scientists & engineers	Biotech R&D investment per number of current patents held*
>15,000	19.6	169,037	423,778	1,430,250	41.3	140,451	303,680	589,630
2,501–15,000	24.2	101,913	575,825	871,720	42.3	115,631	273,856	1,015,841
501–2,500	35.2	120,612	642,038	597,069	28.2	85,124	417,575	735,612
51–500	85.4	154,796	427,077	600,963	181.1	133,982	313,910	609,200
11–50	194.4	150,898	343,179	365,483	332.1	105,263	228,786	384,613
1–10	200.5	190,861	262,008	276,829	117.2	63,271	96,917	200,000
Total	33.4	133,329	479,935	703,187	157.4	103,782	234,141	450,307

*Of the 884 R&D reporting firms reported 0 or more patents. The remaining 9% did not respond to the question regarding patents.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Not surprisingly, other R&D intensity measures—such as the ratios of net biotech sales to biotech employees and to biotech scientists and engineers—also exceed national averages and all other industry sectors. For example, in terms of biotech expenditures per biotech employee, respondents spent an average of $133,329 per employee, more than ten times the rate of U.S. R&D companies generally, which spent on average $11,310 per employee in 2000.[102]

[102] Most recent data available, *U.S. Corporate R&D Investment, 1994–2000 Final Estimates*.

CHAPTER 6
EMPLOYMENT AND WORKFORCE

The *Critical Technology Assessment* survey included 11 questions about the respondent's current workforce, including the occupational composition of workers engaged in biotechnology R&D activities, difficulties finding workers, future recruiting needs, and approaches employed to meet these needs.[104] Respondents indicated that workers with biotechnology-related responsibilities accounted for about 11% of their total workforce of 1.1 million employees. Survey results also suggest that while the vast majority of companies engaged in biotech-related activities are small businesses, employment is concentrated in large companies. In addition, biotech-related employment seems to be highly concentrated in a handful of states, though companies engaged in biotech-related activities can be found in virtually every state of the nation. This chapter provides further analysis of the information provided by respondents or a subset of these firms, as noted.[105]

Occupational Employment

Survey data indicate that employees with biotechnology-related responsibilities accounted for almost 11.5% of respondents' FTEs in 2001/2002.[106] Respondents with fewer employees are more likely to be dedicated biotechnology firms, and the majority of their FTEs have biotechnology-related responsibilities (Figure 6.1).

Respondents' employees had a wide variety of biotechnology responsibilities, including biotech research and development activities, as well as administration and production. For purposes of this report, the term "biotech-related technical workers" includes employees with biotech-related responsibilities who are scientists, engineers, science and clinical laboratory technicians, and R&D-focused computer specialists.[107] These broad categories include many more specialized fields as well (Table 6.1).

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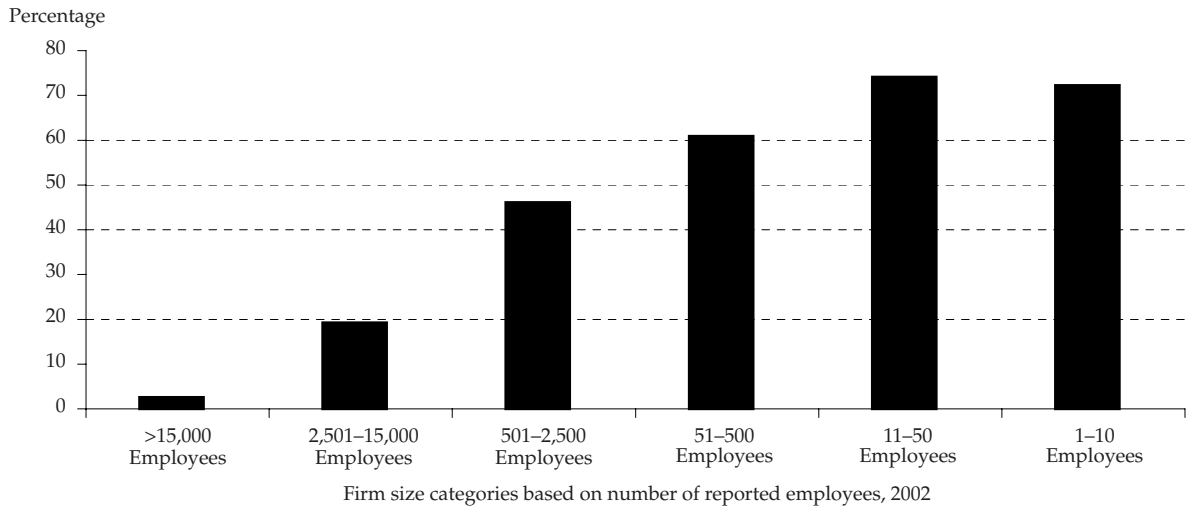
[104] *CTA,* questions 12–20, pages 4–7.

[105] Data presented in this chapter identify the number of firm responses included in each tabulation and do not reflect national workforce estimates. Also, all growth rates for biotech technical occupations were calculated based on a subset of the 850 firms that responded to *CTA,* question 14 for all three years.

[106] Firms did not specify the year for which data were provided in *CTA,* questions 12 and 13.

[107] The occupational analysis in this chapter focuses on firms' responses to questions about employees in occupations involved in biotechnology R&D activities (biotech-related technical workers) to minimize possible misrepresentations caused by double-counting in some survey responses. The total number of employees reported to have biotechnology-related responsibilities segregated by occupational category (*CTA,* question 14, page 4) did not equal the total number of FTEs with biotechnology-related responsibilities (*CTA,* question 13, page 4). It appears likely that some firms' answers to question 14 may double-count workers who perform more than one job. For example, a scientist who is also a manager may have been counted as both.

Figure 6-1: Ratio of Biotech Employees to Total Employees, by Firm Size Category



Firm size categories based on number of reported employees, 2002

Table 6.1: Examples of Biotech-related Technical Workers Involved in Research and Development Activities

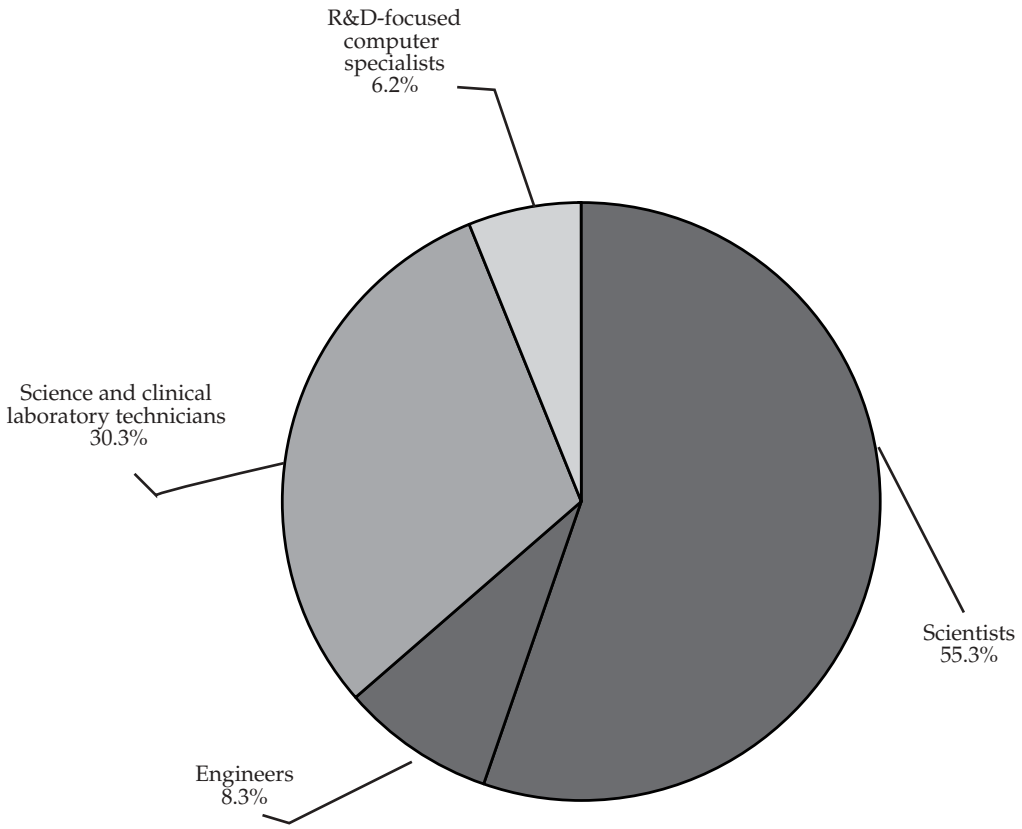
Scientists	Engineers	Science and clinical laboratory technicians	R&D-focused computer specialists
Biologists	Biomedical engineers	Biological/agricultural technicians	Computer scientists
Geneticists	Agricultural engineers	Medical and clinical laboratory technicians	Scientific programmers
Biochemists	Environmental engineers	Assay analysts	Bioinformatics specialists
Biophysicists	Chemical engineers	Food science technicians	Food service engineers
Biomedical scientists		Plant breeders	

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

While most of the survey's 1,031 respondents were small businesses (89.5% have 500 or fewer employees and 59% have 50 or fewer employees), only about 38% of biotech-related technical workers were employed by companies with 500 or fewer employees in 2002.[108]

Biotechnology-related occupations are knowledge-based, and most biotechnology-related employees are highly educated. Of the over 66,000 biotech-related technical workers employed by respondents,[109] scientists accounted for more than half (55%), and science and clinical laboratory technicians accounted for another 30%; engineers (8%) and R&D-focused computer specialists (6%) comprised the remainder (Figure 6.2).

Figure 6.2: Biotech-related Technical Employment by Occupation, 2002



Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Technology in U.S. Industry,* question 14, p. 4, August 2002.

[108] Six firms reported zero employees or skipped these questions.

[109] Firms reported contracting out only a small percentage of their workforce. See discussion later in this chapter.

In 2002, engineers constituted only 4.7% of the total in-house biotech-related technical workforce of companies with 50 or fewer employees, compared to 9.8% of the workforce of companies with more than 500 employees. However, for companies with fewer than 50 employees, scientists constituted a slightly larger share of the technical workforce—which is consistent with the more research-focused nature of smaller firms.

Respondents also were asked to identify employees with biotech-related responsibilities in administration and production—specifically legal workers, production workers, supervisors, and managers. In 2002, general operations, marketing, and financial managers made up almost half (48%) of these other in-house workers. Another 9% were production managers and supervisors. About 40% were production workers, including those in agriculture and aquaculture. Legal workers, including lawyers and paralegals, accounted for only about 4% of survey firms' administrative and production workforce. This may be because lawyers and other legal workers involved in intellectual property and regulatory issues often do not work directly for the biotech companies themselves. Rather, companies (especially smaller firms) are likely to engage the services of law firms specializing in this type of work on an as-needed basis.

The Technical Workforce

The population of companies engaged in biotechnology is dynamic, and growth in the biotechnology-related workforce has been vigorous. Among 850 companies that reported occupational employment for 2000, 2001, and 2002, the biotech-related technical workforce grew at an average annual rate of 12.3%.[110] Companies with 50 to 499 employees experienced the fastest growth in their biotech-related workforce, with an average annual increase of 17.3%, while the growth rate among larger companies was 6.2%, or about half of the overall rate (Table 6.2). However, even this rate outpaced all U.S. nonfarm payroll employment, which remained essentially constant during the period.

Table 6.2: Annual Growth Rate of the Biotechnology-related Technical Workforce by Firm Size Category, 2000–2002

Less than 50	12.8%
50–499	17.3%
500–9,999	11.9%
10,000 or more	6.2%

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Technology in U.S. Industry,* August 2002.

Most growth in technical occupations (81.7%) occurred in companies with 50 to 9,999 employees (Table 6.3). Companies at either end of the employment spectrum (e.g., those with fewer than 50 or more than 10,000 employees) did not contribute as significantly to the total number of new biotech-related technical workers.

The fastest growing technical occupation was R&D-focused computer specialists, a category that grew at an annual rate of 21.8%.[111] Science and clinical labora-

[110] See Appendix B for an explanation of growth rate methodology.

[111] For a discussion of the field of bioinformatics, see the report *Digital Economy, 2003,* by Economic Statistics Administration, U.S. Department of Commerce, 2003.

tory technicians grew at an annual rate of 13.8%; the growth rate for scientists and engineers was 10.8% and 10.7%, respectively (Figure 6.3).

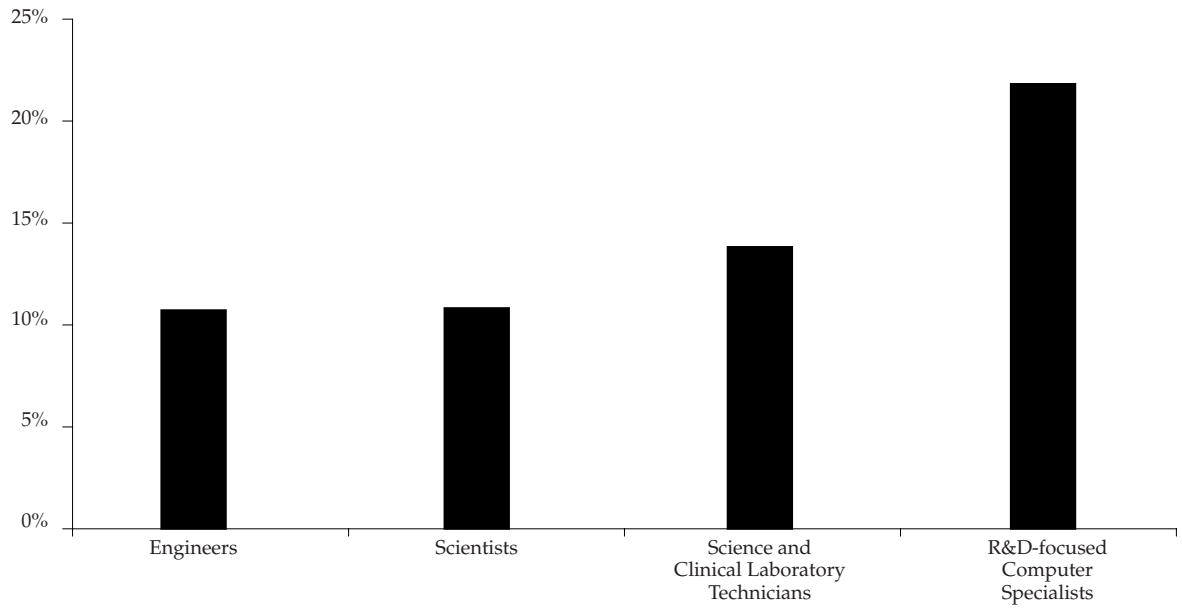
Although R&D-focused computer specialists accounted for the highest average annual rate of growth, the largest growth in absolute numbers of new technical workers was among scientists, a category that added 5,939 new jobs during the 2000–2002 period. Following this lead were science and clinical laboratory technicians (4,337), R&D-focused computer specialists (1,236), and engineers (910), as shown in Figure 6.4.

Table 6.3: Additional Biotechnology-related Technical Employment by Firm Size Category, 2000–2002

Number of Employees	Number of New Technical Workers	Share of New Technical Workers (%)
Less than 50	944	7.6
50–499	5,191	41.8
500–9,999	4,959	39.9
10,000 or more	1,328	10.7

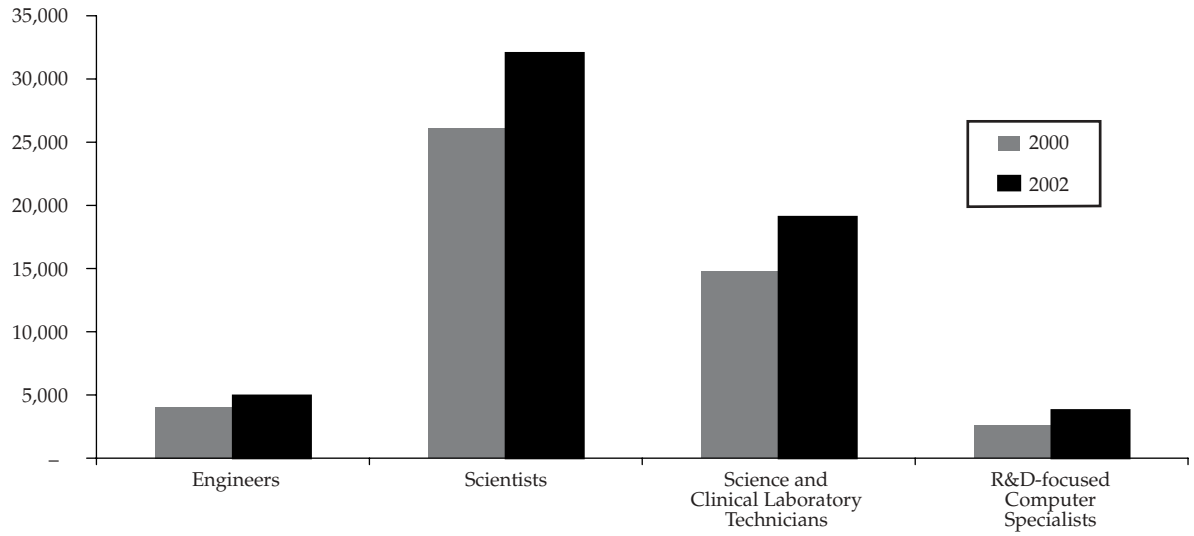
Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Technology in U.S. Industry,* August 2002.

Figure 6-3: Annual Growth Rate in Biotech-related Technical Occupations, 2000–2002



Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Technology in U.S. Industry,* question 14, p. 4, August 2002.

Figure 6.4: Employment in Biotechnology-related Technical Occupations, 2000–2002



Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Technology in U.S. Industry,* question 14, p. 4, August 2002.

Geographic Distribution

For the 720 companies with fewer than 100 employees,[112] the survey confirmed that the U.S. biotech-related workforce is highly concentrated. Six states—California, Massachusetts, Maryland, North Carolina, Pennsylvania, and New Jersey—accounted for about 68% of biotechnology-related employment in these businesses in 2002 (Table 6.4).

Other studies suggest that factors critical to the development of a strong regional biotechnology presence include the availability of venture capital and local entrepreneurship, a strong research presence, and proximity to a pool of highly skilled personnel.[113]

[112] Analysis was limited to smaller firms in order to assess employment distribution by state more accurately, since a large firm headquartered in one state may actually have employees distributed throughout the country. This distribution would not be evident if a firm's headquarters completed the *CTA* for all company operations. See Chapter 2 for additional geographic information about respondents.

[113] For example, Joseph Cortright and Heike Mayer, "Signs of Life: The Growth of Biotechnology Centers in the U.S.," Washington, D.C.The Brookings Institution Center on Urban and Metropolitan Policy, 2002.

Resources for Meeting Workforce Requirements

Companies engaged in biotech-related research and manufacturing indicated a strong reliance on recruiting from local labor markets to meet their biotech workforce requirements.[114] Approximately two-thirds of respondents (63.9%) stated that recruitment from the local labor market provided 75% or more of their employees, while more than a third (37.3%) indicated that local labor markets accounted for more than 95% of their employees (Table 6.5). Local labor markets provided about 77% of the workforce for respondents with defense contracts.[115]

Table 6.4: States with Largest Biotech-related Employment

Based on Employment in Responding Firms with Fewer than 100 Workers	
California	4,418
Massachusetts	1,586
Maryland	1,195
North Carolina	758
Pennsylvania	705
New Jersey	703
Total, top 6 states	9,365
Total, all states	13,789

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Technology in U.S. Industry.*

Table 6.5: Number and Percentage of Firms' Biotechnology Workforce

Source/ Share of Workforce	Less than 10%		Less than 25%		25–75%		More than 75%		More than 95%		Total
Recruited from the local labor market/U.S. firms	100	9.7%	160	15.5%	212	20.6%	658	63.9%	384	37.3%	1,030
Recruited from U.S. four-year degree or postgraduate degree	452	43.9%	653	63.4%	187	18.2%	190	18.4%	86	8.3%	1,030
Recruited from U.S. two-year degree or junior colleges, or technical schools	891	86.5%	1,014	98.4%	14	1.4%	2	0.2%	2	0.2%	1,030
Foreign employees with a U.S. visa or work permit	693	67.3%	959	93.1%	66	6.4%	5	0.5%	3	0.3%	1,030
Foreign employees residing abroad	1,005	97.6%	1,022	99.2%	3	0.3%	5	0.5%	1	0.1%	1,030

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

[114] Companies were asked to provide an estimate of the percentage of their workforce recruited from various sources. *CTA*, question 17, page 6.

[115] For purposes of this chapter, "defense contractors" refers to the 105 companies answering the survey that held defense contracts in the last five years. *CTA*, question 39, page 16.

For nearly two-thirds of respondents (63.4%), recruitment from four-year or postgraduate degree-granting institutions provides less than 25% of their workforce requirements. Only 18.4% of companies fill more than 75% of their workforce requirements from these sources. Recruitment from two-year community/junior colleges and technical schools provide even fewer workers: 86.5% stated that they relied on these institutions for less than 10% of their workforce requirements, while 98.4% of companies indicated that these institutions provided less than 25% of their workforce requirements.

Domestic and Foreign Outsourcing

From 2000 to 2002, only a small percentage of respondents' biotechnology-related technical workforce requirements were met through contracting. In 2002, more than 96% of biotech-related technical workers were employed in-house (Table 6.6). Outsourcing—both domestic and foreign—accounted for 3.9% of the biotech-related technical workforce, with domestic outsourcing accounting for 3.3% (2,053 workers) and foreign outsourcing accounting for only 0.6% (347 workers).

Table 6.6: Share of Biotech-related Technical Workforce Working under Contracts, 2000–2002 (%)

	2000	2001	2002
In the United States	3.9	2.8	3.3
Outside the United States	0.7	0.5	0.6
Total	4.6	3.3	3.9

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

A large majority of companies responding to the survey reported a low reliance on the use of outsourcing to meet their workforce requirements. More than three-fourths (77%) stated that outsourcing to domestic firms provides l0% or less of their workforce needs, while 83% stated that outsourcing to foreign firms operating abroad provides l0% or less of their workforce. Less than 4 percent of respondents (40 firms) indicated that they use domestic or foreign outsourcing to meet half or more of their workforce needs. Of these companies, three-fourths had 50 or fewer employees.

Outsourcing appears to be used disproportionately to meet companies' requirements for R&D-focused computer specialists. While R&D-focused computer specialists accounted for only 6.3% of the in-house technical workforce of company respondents in 2002, they accounted for 28.8% of the workers under contract abroad and 12.4% of those employed under domestic contracts (Table 6.7). These ratios were similar for 2001. In contrast, a smaller percentage of companies' requirements for scientists and for science and clinical laboratory technicians were met through outsourcing.

Less than 6% of firms reported obtaining technical workers through foreign outsourcing. Less than 4% reported obtaining R&D-focused computer specialists through foreign outsourcing, with those that did reporting an average of seven employees per company and a median of two employees per company.

Table 6.7: Technical Workforce Occupational Portfolio, In-house and Contract, 2002

	In-house (%)	Contract (%)	
		Domestic	Foreign
Engineers	8.3	9.6	9.8
R&D-focused Computer Specialists	6.3	12.4	28.8
Science & Clinical Laboratory Technicians	31.9	36.1	16.7
Scientists	53.5	41.9	44.7
Total	100.0	100.0	100.0

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

While about half (516) of the 1,031 *CTA* respondents stated that they were contemplating outsourcing domestically with U.S. firms/facilities, only a little more than 26% (272) stated that they were contemplating outsourcing to foreign firms/facilities.

Finally, survey results indicate that companies that are involved in biotechnology and that accept defense work may be more likely to contract work to U.S. colleges, universities, and other non-profit organizations than companies that do not handle defense work. While more than 50% of responding firms that have held defense contracts reported working with such groups (28 of 54), only 30% of respondents that do not have defense contracts reported doing so.

Future Workforce Needs

Access to highly skilled workers is critical to any high-tech company. According to survey respondents, companies with fewer than 50 employees have a much more difficult time meeting their biotech workforce needs. Nearly half of these companies reported that more than 20% of their biotech-related positions had been unfilled for more than three months, compared with less than 1% of positions for companies with more than 50 employees.

While smaller companies engaged in biotech-related activities have a more difficult time meeting their workforce needs than do larger companies, they are less likely to use the variety of mechanisms available to address this challenge. Large companies are more likely to be using or planning to use a wide variety of mechanisms to meet their requirements for skilled workers.

Comparing companies with more than 50 employees to those with fewer than 50 employees, larger companies are

- almost four times as likely to use recruiting bonuses,
- three times as likely to use overtime incentives,

- nearly three times as likely to use foreign recruiting, and
- twice as likely to establish foreign facilities to gain access to skilled workers.

Contrasting very large companies—those with more than 10,000 employees—with very small companies—those with fewer than 20 employees—accentuates these differences. Compared to very small companies, very large companies are

- more than seven times as likely to use recruiting bonuses,
- five times as likely to use overtime incentives,
- seven times as likely to use foreign recruiting, and
- more than four times as likely to establish foreign facilities to gain access to skilled workers.

It is striking to note that companies that reported facing greater difficulties filling their open positions (20% or more unfilled for more than three months) were more likely to rely on foreign recruiting, establishing foreign facilities to gain access to workers, and subcontracting to another company or academia to try to fill open positions (Table 6.8) than companies reporting little trouble filling their open positions (5% or less unfilled for more than three months). Both groups reported that in-house training and increased salaries are the two mechanisms most often employed to ensure a sufficient number of adequately skilled workers and professionals for their firm.[116]

Table 6.8: Share of Companies Using Selected Mechanisms to Meet Workforce Demands

Mechanism	Companies Reporting Difficulty Filling… Less than 5% of positions	More than 20% of positions
In-house training	89.5%	76.9%
College recruiting	68.4%	38.5%
Increased salaries	67.7%	65.4%
Overtime incentives	10.5%	0.0%
Foreign recruiting	9.8%	19.2%
Establishing foreign facilities	11.3%	15.4%
Recruiting bonuses	57.9%	11.5%
Enhanced benefit plans	57.9%	34.6%
Subcontracting to another company or academia	27.1%	34.6%
Outsourcing	37.6%	19.2%

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

[116] *CTA*, question 20, page 7.

Chapter 7
Competitive Outlook

Given the astounding variety of industries that apply cellular and molecular processes to solve problems, conduct research, and create goods and services, it is clear that the application of new biotechnologies is an integral feature of the national economic fabric. The fabric is still being woven, however. Operating incomes for the biotechnology-related business lines of most small companies are low or in the red, some applications continue to raise ethical considerations, and few other industrial platforms must meet a similarly stringent degree of regulatory oversight. Yet despite great complexity, financial fragility, and difficult business development hurdles, the development and adoption of biotechnologies is a critical component of national economic competitiveness, social well-being, and security. In an effort to assist policymakers, understanding of what may be helpful in sustaining the growth and evolution of biotechnology in U.S. industries, the *Critical Technology Assessment* asked nine questions about barriers perceived by biotechnology companies, firms' near-term competitive business strategies, and their perspectives on the future. Following is a summary of respondents' thinking about these questions.

Barriers to Business Competitiveness

The *Critical Technology Assessment* asked companies to identify barriers that impede advancement of biotechnology research or product commercialization and to indicate the severity of those impediments.[117] Results for survey respondents as a group confirmed the importance of transparent, timely regulatory regimes and sufficient, steady start-up capital (Table 7.1).

The preponderance of regulatory concerns reflects, in part, the comprehensive regulatory regime faced by the vast majority of respondents that work in biotechnology application areas subject to some type of regulatory approval process. In fact, some type of regulatory oversight is likely to be exercised for most products and processes associated with six out of the seven application areas discussed in Chapter 3.[118]

Almost 20 years ago, the federal government recognized the need to examine the national regulatory structure that was in place for new biotech products and processes. In July 1986, the White House Office of Science and Technology Policy (OSTP) established an interagency

[117] *CTA*, question 37, page 15.

[118] Many companies that identified the "other" category of biotechnology applications are not likely to be subject to regulatory approval, as their businesses are focused on development of hardware, software, and tools for biotech research companies.

[119] 51 Federal Register 23302, June 26, 1986.

Table 7.1: Company Perceptions of Barriers to Advancement

	Fraction of respondents saying: high barrier (%)	no/low barrier (%)
Regulatory approval process and costs	58.5	23.6
Research costs	53.2	19.0
Access to start-up capital	52.8	34.8
Patent rights held by third parties	34.9	41.8
Patent fees and approval process	34.8	39.3
Liability concerns/insurance costs	29.2	44.0
Marketing costs	26.3	46.4
Lack of understanding or interest by U.S. govt. policymakers	25.5	49.4
Lack of patent protection abroad for product/process	23.0	53.0
Antiquated rules and regulations	21.3	54.0
Insufficient or unstable government funding for R&D	20.1	61.0
Shortage of approved U.S. manufacturing facilities	17.0	64.9
Government procurement practices/regulations	16.1	65.3
Size of market	16.0	62.8
Lack of qualified biotechnology employees	15.3	56.4
Access to international markets	14.2	64.3
Access to technology	13.1	40.7
Public acceptance/ethical considerations	11.9	67.9
Unfair foreign laws	11.0	75.3
Export control regulations	10.2	70.9
Transportation regulations (incl. hazardous material handling regulations)	10.0	72.3
Unfair U.S. laws	9.3	75.9
Import regulations	8.4	75.3
Unfair competition	8.0	77.0
Distribution and transportation costs	7.8	76.4
Local zoning	6.7	80.1
Access to information	5.9	71.4
Antitrust laws	3.6	84.0
Construction delays	2.8	90.1
Equipment shortage	2.7	86.4

Depending on the barrier, 716 to 881 of the 1,031 companies responded to these questions.

Respondents were asked to rate each barrier on a 1 to 5 scale. 1 = no barrier and 5 = high barrier, with other values reflecting levels in between. The fraction of respondents reported in the "high" barrier level is the sum of 4 and 5 responses. That for the "no/low" barrier level is the sum of 1 and 2 responses.

"coordinated framework"[119] clarifying agency regulatory responsibilities with respect to biotechnology products and processes.[120] Oversight of biotech products associated with human and animal health is exercised by several offices of the U.S. Department of Health and Human Service's Food and Drug Administration (HHS/FDA), according to regulations found in the Federal Food, Drug, and Cosmetic Act.[121] Recently, in an effort to streamline the regulatory process for biotech companies and in recognition of changes in product development, the FDA announced the merger of two agency offices[122]—the Center for Drug Evaluation and Research (CDER)[123] and the Center for Biologics Evaluation and Research (CBER)[124]—a move that has met with cautious approval by a number of U.S. biotechnology firms.[125] The agency is also sensitive to firms' need for expeditious review of biotech-related applications.[126]

Regulation of certain other biotech products falls under the authority of other agencies, most notably the United States Department of Agriculture (USDA) and the Environmental Protection Agency (EPA). Several USDA bureaus interact with biotechnology companies that are seeking field-testing or marketing approval of genetically engineered organisms. One of the primary USDA monitoring and regulating bodies is the Animal and Plant Health Inspection Service (APHIS), which regulates certain animal health-related biologics, as well as the movement, importation, and field-testing of genetically engineered organisms. Also of importance is the Food Safety Inspection Service (FSIS), which has responsibility for the safe use of engineered domestic livestock and poultry and products derived from them.[127]

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[120] New regulatory agencies specific to biotechnology did not emerge, in part because of conclusions by the National Academy of Sciences that "products of recombinant DNA technology are not inherently more risky than those made by conventional production methods." (See *Biotechnology: Science, Engineering, and Ethical Challenges in the 21st Century:* pp. 223-260. National Academies of Sciences, Joseph Henry Press, 1996).

[121] 21 USC 9, passed 1938, last amended 1992. See http://www4.law.cornell.edu/uscode/21/ch9.html (viewed July 9, 2003).

[122] See http://www.fda.gov/bbs/topics/NEWS/2003/NEW00880.html (viewed July 30, 2003).

[123] The CDER approves prescription and over-the-counter drugs, both brand-name and generic, and determines that the health benefits of new drugs outweigh known risks. See http://www.fda.gov/cder/about/faq/default.htm#1 (viewed August 16, 2003).

[124] The CBER (www.fda.gov/cber) regulates biological products according to Section 351 of the Public Health Service (PHS) Act (42 USC 351) and specific sections of the Federal Food, Drug, and Cosmetic Act.

[125] Interviews with biotech company officials, July 16 and July 22, 2003.

[126] Median approval times vary according to the type of product and other factors. For more detailed information, see http://www.fda.gov/bbs/topics/news/2003/beyond 2002/report.html (viewed August 13, 2003).

[127] Statutory authority given by the Federal Meat Inspection Act (FMIA), 21 USC 601-691; Poultry Products Inspection Act (PPIA), 21 USC 451-471; and Egg Products Inspection Act (EPIA), 21 USC 1031-1056.

EPA regulates microbes and certain novel microorganisms intended for commercial use, including "microorganisms formed by deliberate combinations of genetic material from different taxonomic genera."[128] In July 2001 EPA promulgated three rules that would "formalize and strengthen EPA's framework for federal oversight of a class of pesticides produced and used in living plants."[129]

As might be expected, biotechnology firms whose applications do not require lengthy and expensive clinical trials prior to regulatory approval indicated slightly different concerns than respondents in human and animal health and agriculture. For example, companies working in industrial and agricultural-derived processing applications named "research costs" as their most significant barrier and also flagged "unfair foreign laws" and "government procurement" among their top impediments. Agricultural and aquacultural application respondents also cited "unfair foreign laws" and added "public acceptance/ethical considerations" to their list of most significant barriers. Respondents involved in environmental remediation cited "antiquated rules and regulations," "unfair U.S. laws," "government procurement," and "access to international markets."

Between 11% and 14% of all respondents indicated that access to international markets and unfair foreign laws posed a "high" barrier to advancement of biotechnology-related research or product commercialization.[130] Domestic export control regulations and import regulations presented a "high" barrier for about 10% of respondents.[131]

Access to Capital

Among all but the very largest respondents in all application categories, access to capital was consistently one of the most important barriers. Survey responses indicate that the significance of capital access as a barrier varied between large companies and smaller firms, with smaller

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[128] EPA's regulatory authority resides in three federal statutes: the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), 7 USC 136-136y, as amended by the Food Quality Protection Act, *supra;* the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 USC 321, 346a, as amended by FQPA (FWPA); and the Toxic Substance Control Act (TSCA), 15 USC 2601-2692. Microbial regulation is authorized by TSCA.

[129] Environmental Protection Agency, Plant-Incorporated Protectant Rules, http://www.epa.gov/scipoly/pips.htm (viewed July 12, 2003).

[130] Respondents were not asked to submit specific instances of trade barriers. The Office of the United States Trade Representative compiles an annual Foreign Trade Barriers Report, which describes country practices that impede trade and investment. Trade barriers applicable to health-related applications include (1) the length of time that it takes to obtain approved prices for medical products and (2) insufficient protection for intellectual property rights, including patents on biotechnological inventions and pharmaceuticals, and protection of confidential test data submitted during the regulatory approval process. In agricultural biotechnology, barriers include moratoria on approval of biotech-derived crops and processed foods, and onerous labeling requirements.

[131] No specifics on the particular country or hurdles were requested or provided. The length of time it takes to process applications for products or know-how that have military applications could add to delays in exporting. Export regulations are enforced by the Departments of State and Commerce. As previously discussed, the FDA, USDA, and EPA regulate the importation of products for health and safety.

firms more frequently indicating that it was a major impediment. Smaller respondents (those with 500 or fewer employees) identified both venture capital and angel capital as important sources of funds for their R&D activities. Government loans and grants (both federal and state) were also mentioned (see Chapter 2 for more information).

Although the amount of venture capital invested in biotechnology firms declined in both 2001 and 2002, biotech firms received an increasing share of venture capital funds (Table 7.2). However, the absolute amount of venture capital flows does not tell the entire story. Both the average size of investment and the stage at which investors are willing to support start-up firms are important. Currently, there appears to be some concern that most venture capital money is flowing more to later-stage products and less to technology platforms that may be used to develop multiple products.[132]

Table 7.2: Venture Capital Investment, 2000–2002 ($ millions)

	2000	2001	2002
Total $	106,225	40,801	16,944
Biotech $	4,259	3,226	2,832
Total number of deals	8,138	4,635	3,039
Total number of biotech deals	331	298	287

Source: The MoneyTree Survey from PricewaterhouseCoopers, Thompson Venture Economics, and the National Venture Capital Association, http://www.pwcmoneytree.com/moneytree/nav.jsp? page=historical (viewed July 30, 2003).

Intellectual Property

Also frequently cited by survey respondents as barriers to the advance of biotech research and product commercialization are issues related to intellectual property protection. Thirty-five percent of the respondents identified patent fees and the patent approval process as a barrier; a similar fraction identified patent rights held by third parties.

IP protections are a critical underpinning for a vigorous pace of innovation. Prevailing principles and mechanisms of national IP regimes play an important role in helping to establish value for the results of R&D. They open doors to financing and capital markets, which are also important business considerations. IP rights—notably through patents—are essential in providing sufficient incentives for the private sector to raise capital and provide investment funding for biotech R&D. Yet sorting out IP rights also imposes significant complexity and costs on the operation of R&D programs.

The depth of the present debate on what IP policies should prevail when it comes to patent policy and biotech R&D, and the lack of consensus on viable solutions, create uncertainties for biotech businesses. Recent evidence indicates that investment in biotechnology firms is particularly sensitive to capital and equity markets' perceptions of national patent policy. So it is not surprising that many survey respondents mentioned IP issues as significant challenges.

[132] For a discussion of all types of biotech financing see, *Biotech 2003: Revaluation and Restructuring* (San Francisco: Burrill and Company).

Several developments have worked to increase the complexity of biotech business activities and increase the required time and resources (such as expenses for legal representation) to move company R&D efforts forward. For example, as private companies, universities, and other parties involved in research aggressively pursue a full range of protection under U.S. IP laws, R&D companies are more often required to negotiate agreements with other IP holders to gain access to necessary technology or to form collaborative research and business teams. At the same time, contests for IP rights have become a good deal more competitive and increased the flow of claims, counterclaims, and infringement suits.

More broadly, the way in which long-standing IP laws intersect with new biotech-related products and processes uncovered through R&D is a matter of growing controversy. The products of modern genetic research may be considered, depending on their application, either as revealed aspects of nature (which generally are not protectable by U.S. patent law) or as inventions and useful devices (which are protected). The solutions to these developments, with both challenging and unique questions for policy, spark significant disagreements among the myriad stakeholders.[133] There is agreement on the need for a balanced system of policies that provide market incentives that can facilitate creative research and encourage further discovery and disclosure, but not unduly restrict dissemination of these discoveries, hinder the circulation of important scientific ideas, or dilute ownership to the point that the use of underlying scientific and technological advances would be slowed.

Competitive Strategies

For respondents as a group, near-term business strategies primarily are focused on developing technologies that can be licensed to other companies (the choice of 53% of respondents) and acquiring technologies from other companies through licensing arrangements (47%) or joint venture arrangements (23%) (Table 7.3).

Of course, the benefits of these activities differ from each other; "licensing-out" technology generally provides revenue to a company, while "licensing-in" often provides or enhances a new type of technology or technology platform. The high number of companies that are planning to license-in technology, combined with the high number that plan to refocus R&D activities or product development (43% and 39%, respectively) suggests that many firms may not yet be fully committed to a specific biotechnology-related product or line of business. It also may reflect a business strategy for coping with "patent thickets" in situations where multiple owners hold important underlying patents related to firms' business development strategy. Future survey efforts could provide insight into the development of nascent biotechnologies and technology platforms and the factors that influence those business decisions.

[133] For a recent and useful set of papers discussing these issues and competing points of view, see the special edition of *Academic Medicine* (Journal of the Association of American Medical Colleges), Vol. 77, No. 12, Dec. 2002, "Public versus Private Ownership of Scientific Discovery: Legal and Economic Analyses of the Implications of Human Gene Patents," David Korn and Stephen J. Heinig, editors.

Table 7.3: Anticipated Near-term Shifts in Competitive Strategies, Overall

Strategic Response to Business Conditions	Number of companies indicating this action	Percentage of companies responding
No change in strategic response	54	5.2
License-out technology	548	53.2
Expand operations	530	51.5
License-in technology	487	47.3
Enter product trials	463	45.0
Refocus R&D activities	439	42.6
Launch a new product	410	39.8
Refocus product development	402	39.0
Increase recruitment efforts for U.S. workers	338	32.8
Outsource production	251	24.4
Expand into foreign markets	247	24.0
Form a joint venture	234	22.7
Merge with other company	121	11.7
Acquire a company	113	11.0
Downsize operations	112	10.9
Recruit employees abroad	102	9.9
Establish facilities abroad	78	7.6
Establish additional R&D collaborations	1	0.1
Other	21	2.0
No response	10	1.0

1,030 of 1,031 companies in the survey responded to this question.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Table 7.3, continued: Anticipated Near-term Shifts in Competitive Strategies, Human Health Applications

Strategic Response to Business Conditions	Number of companies indicating this action	Percentage of companies responding
No change in strategic response	26	3.3
License-out technology	468	60.0
Expand operations	423	54.2
License-in technology	396	50.8
Enter product trials	398	51.0
Refocus R&D activities	348	44.6
Launch a new product	293	37.6
Refocus product development	300	38.5
Increase recruitment efforts for U.S. workers	276	35.4
Outsource production	208	26.7
Expand into foreign markets	169	21.7
Form a joint venture	190	24.4
Merge with other company	88	11.3
Acquire a company	85	10.9
Downsize operations	83	10.6
Recruit employees abroad	84	10.8
Establish facilities abroad	60	7.7
Establish additional R&D collaborations	1	0.1
Other	15	1.9
No response	6	0.8

780 of the 780 companies with applications in this area responded to this question.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Table 7.3, continued: Anticipated Near-term Shifts in Competitive Strategies, Animal Health Applications

Strategic Response to Business Conditions	Number of companies indicating this action	Percentage of companies responding
No change in strategic response	6	4.2
License-out technology	84	58.3
Expand operations	78	54.2
License-in technology	76	52.8
Enter product trials	71	49.3
Refocus R&D activities	70	48.6
Launch a new product	76	52.8
Refocus product development	69	47.9
Increase recruitment efforts for U.S. workers	45	31.3
Outsource production	48	33.3
Expand into foreign markets	45	31.3
Form a joint venture	40	27.8
Merge with other company	15	10.4
Acquire a company	21	14.6
Downsize operations	19	13.2
Recruit employees abroad	19	13.2
Establish facilities abroad	16	11.1
Establish additional R&D collaborations	0	0.0
Other	4	2.8
No response	0	0.0

144 of the 144 companies with applications in this area responded to this question.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Table 7.3, continued: Anticipated Near-term Shifts in Competitive Strategies, Agriculture and Aquaculture/Marine Applications

Strategic Response to Business Conditions	Number of companies indicating this action	Percentage of companies responding
No change in strategic response	10	7.8
License-out technology	67	52.3
Expand operations	59	46.1
License-in technology	63	49.2
Enter product trials	48	37.5
Refocus R&D activities	63	49.2
Launch a new product	55	43.0
Refocus product development	55	43.0
Increase recruitment efforts for U.S. workers	42	32.8
Outsource production	32	25.0
Expand into foreign markets	43	33.6
Form a joint venture	37	28.9
Merge with other company	14	10.9
Acquire a company	24	18.8
Downsize operations	18	14.1
Recruit employees abroad	20	15.6
Establish facilities abroad	13	10.2
Establish additional R&D collaborations		0.0
Other	6	4.7
No response	2	1.6

128 of the 128 companies with applications in this area responded to this question.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Table 7.3, continued: Anticipated Near-term Shifts in Competitive Strategies, Marine and Terrestrial Microbial Applications

Strategic Response to Business Conditions	Number of companies indicating this action	Percentage of companies responding
No change in strategic response	2	4.9
License-out technology	26	63.4
Expand operations	22	53.7
License-in technology	16	39.0
Enter product trials	17	41.5
Refocus R&D activities	21	51.2
Launch a new product	24	58.5
Refocus product development	19	46.3
Increase recruitment efforts for U.S. workers	13	31.7
Outsource production	15	36.6
Expand into foreign markets	19	46.3
Form a joint venture	15	36.6
Merge with other company	4	9.8
Acquire a company	7	17.1
Downsize operations	8	19.5
Recruit employees abroad	7	17.1
Establish facilities abroad	8	19.5
Establish additional R&D collaborations	0	0.0
Other	0	0.0
No response	1	2.4

41 of the 41 companies with applications in this area responded to this question.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Table 7.3, continued: Anticipated Near-term Shifts in Competitive Strategies, Industrial and Agricultural-derived Processing Applications

Strategic Response to Business Conditions	Number of companies indicating this action	Percentage of companies responding
No change in strategic response	8	6.1
License-out technology	70	53.0
Expand operations	70	53.0
License-in technology	63	47.7
Enter product trials	54	40.9
Refocus R&D activities	70	53.0
Launch a new product	74	56.1
Refocus product development	68	51.5
Increase recruitment efforts for U.S. workers	44	33.3
Outsource production	44	33.3
Expand into foreign markets	48	36.4
Form a joint venture	46	34.8
Merge with other company	11	8.3
Acquire a company	30	22.7
Downsize operations	19	14.4
Recruit employees abroad	17	12.9
Establish facilities abroad	13	9.8
Establish additional R&D collaborations	0	0.0
Other	1	0.8
No response	1	0.8

132 of the 132 companies with applications in this area responded to this question.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Table 7.3, continued: Anticipated Near-term Shifts in Competitive Strategies, Environmental Remediation and Natural Resource Recovery Applications

Strategic Response to Business Conditions	Number of companies indicating this action	Percentage of companies responding
No change in strategic response	5	12.2
License-out technology	19	46.3
Expand operations	21	51.2
License-in technology	11	26.8
Enter product trials	11	26.8
Refocus R&D activities	10	24.4
Launch a new product	18	43.9
Refocus product development	9	22.0
Increase recruitment efforts for U.S. workers	15	36.6
Outsource production	10	24.4
Expand into foreign markets	22	53.7
Form a joint venture	12	29.3
Merge with other company	3	7.3
Acquire a company	6	14.6
Downsize operations	3	7.3
Recruit employees abroad	8	19.5
Establish facilities abroad	8	19.5
Establish additional R&D collaborations	0	0.0
Other	2	4.9
No response	1	2.4

41 of the 41 companies with applications in this area responded to this question.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Table 7.3, continued: Anticipated Near-term Shifts in Competitive Strategies, Other Applications

Strategic Response to Business Conditions	Number of companies indicating this action	Percentage of companies responding
No change in strategic response	18	11.3
License-out technology	61	38.1
Expand operations	85	53.1
License-in technology	62	38.8
Enter product trials	33	20.6
Refocus R&D activities	55	34.4
Launch a new product	87	54.4
Refocus product development	62	38.8
Increase recruitment efforts for U.S. workers	49	30.6
Outsource production	26	16.3
Expand into foreign markets	45	28.1
Form a joint venture	27	16.9
Merge with other company	21	13.1
Acquire a company	22	13.8
Downsize operations	13	8.1
Recruit employees abroad	12	7.5
Establish facilities abroad	9	5.6
Establish additional R&D collaborations	0	0.0
Other	3	1.9
No response	1	0.6

160 of the 160 companies with applications in this area responded to this question.

Source: U.S. Department of Commerce Technology Administration and Bureau of Industry and Security, *Critical Technology Assessment of Biotechnology in U.S. Industry,* August 2002.

Foreign Markets and Exports

Foreign markets also were noted in companies' immediate competitive strategies. Respondents indicated that Europe was the destination for over half of their biotechnology-related exports in 2001, accounting for approximately $4.5 billion in revenue. Exports to the Asia/Pacific region were next, with $1.9 billion, or about one-quarter of sales, followed by Latin America and Canada (Table 7.4). The leading export markets in terms of individual countries were Japan, Germany, and the United Kingdom.

Not surprisingly, the geographic pattern of export markets tracks trends reported to the U.S. Bureau of the Census by firms involved in pharmaceutical and medicinal applications (drugs, biologics, and in vivo and in vitro diagnostics), under the North American Industry Classification System (NAICS) 3254. In 2001, U.S. exports of these products totaled $18.1 billion, about 60% of which went to Europe (Table 7.5).

Future Expectations

Respondents are generally optimistic about the future, with 76% indicating that they expect competitive prospects for their business operations over the next two years to improve "greatly" or "somewhat."[134] Only 46 out of the 1,031 survey respondents (4.5%) believe their future competitive business prospects will decline "somewhat" or "greatly" over the next two years (Table 7.6). These are generally smaller firms with fewer than 100 employees and no or negative operating income.

Companies working in the application area of environmental remediation and natural resource recovery were particularly optimistic—no respondent indicated that business prospects were likely to decline during the next two years. Respondents working in agriculture and aquaculture/marine applications were the most pessimistic, with nine companies (7.3%) indicating that business prospects were likely to worsen in the near future. In part, this likely reflects the perception of continuing trade barriers in foreign markets.[135]

Table 7.4: Export Revenues by Geographic Region, 2001

Location	2001 ($000)	Percentage of Biotech Exports
Europe	4,483,199	55.81
Asia/Pacific	1,936,751	24.11
Latin America	705,511	8.78
Canada	596,079	7.42
Rest of world	243,755	3.03
Company omissions	66,973	0.83
Total	8,032,268	100.0

Source: CTA, question 31, page 12.

Table 7.5: U.S. Exports of Pharmaceuticals and Medicines, NAICS 3254

Location	2001 ($000)	Percentage of Exports
Europe	10,208,112	60.2
Asia/Pacific	2,515,979	16.2
Latin America	1,503,612	8.3
Canada	2,225,535	12.3
Rest of world	545,410	3.0
Total U.S. Exports	18,117,634	100.0

Source: U.S. Bureau of the Census.

Table 7.6: Expectations of Near-term Business Prospects

"Which of the following best describes the competitive prospects for your business operations over the next two years?"	Number of Companies	Percentage of Total	Cumulative Percentage
Improve greatly	381	37.6	37.6
Improve somewhat	387	38.2	75.8
Remain stable	199	19.6	95.5
Decline somewhat	28	2.8	98.2
Decline greatly	18	1.8	100.0

1,013 of the 1,031 companies in the survey responded to this question.

Source: CTA, question 33, page 13.

[134] *CTA*, question 32, page 13.

[135] *CTA*, question 37, page 15.

DEPARTMENT OF COMMERCE

APPENDIX A
CRITICAL TECHNOLOGY ASSESSMENT OF BIOTECHNOLOGY IN U.S. INDUSTRY SURVEY QUESTIONNAIRE

Note: Any information submitted in response to this survey will be deemed business confidential and exempt from public disclosure in accordance with section 705 of the Defense Production Act of 1950, as amended.

DEPARTMENT OF COMMERCE

BUSINESS CONFIDENTIAL

Ref # B-1

OMB Control # 0694-0119
Expiration Date: 10/31/2002

CRITICAL TECHNOLOGY ASSESSMENT OF BIOTECHNOLOGY IN U.S. INDUSTRY

SCOPE OF ASSESSMENT

The U.S. Department of Commerce, Bureau of Industry and Security (BIS), Office of Strategic Industries and Economic Security, and the Technology Administration, Office of Technology Policy are conducting an assessment of Biotechnology in U.S. Industry. The goals of this assessment are to analyze the economic health and competitiveness of companies that are involved in biotechnology research or production, and to better characterize current and developing commercial and national security related products/processes. Your timely and complete response will assist the participating organizations in their efforts to perform a comprehensive, first-time analysis of this critical area.

RESPONSE TO THIS SURVEY IS REQUIRED BY LAW

This report is required by law (50 U.S.C. App. Sec. 2155). Failure to report can result in a maximum fine of $10,000 or imprisonment up to one year, or both. Information furnished herewith is deemed confidential and will not be published or disclosed except in accordance with Section 705 of the Defense Production Act of 1950, as amended (50 U.S.C. App. Sec. 2155). Section 2061 et. seq. prohibits the publication or disclosure of this information unless the President determines that its withholding is contrary to the national defense. Information will not be shared with any non-government entity, other than in aggregate form, and the information will be protected pursuant to the appropriate exemptions from disclosure under the Freedom of Information Act (FOIA), should it be the subject of a FOIA request.

Notwithstanding any other provision of law, no person is required to respond to nor shall a person be subject to a penalty for failure to comply with a collection of information subject to the requirements of the Paperwork Reduction Act unless that collection of information displays a currently valid OMB Control Number.

BURDEN ESTIMATE & REQUEST FOR COMMENT

Public reporting burden for this collection of information is estimated to average five hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to U.S. Department of Commerce, BIS Reports Clearance Officer, Room 6883, Bureau of Industry and Security, Washington, DC 20230, and to the Office of Management and Budget, Paperwork Reduction Project (OMB Control Number 0694-0119), Washington, DC 20503.

Note: Any information submitted in response to this survey will be deemed business confidential and exempt from public disclosure in accordance with section 705 of the Defense Production Act of 1950, as amended.

BUSINESS CONFIDENTIAL

DEFINITIONS

Biotechnology: The application of molecular and cellular processes to solve problems, conduct research, and create goods and services. It includes a diverse collection of technologies that manipulate cellular, sub-cellular, or molecular components in living things to make products or discover new knowledge about the molecular and genetic basis of life, or to modify plants, animals and micro-organisms to carry desired traits. Such technologies include, but are not limited to: genetic engineering (e.g., recombinant DNA, gene therapy, cloning, antisense); hybridoma technology (to produce monoclonal antibodies); polymerase chain reaction or PCR amplification; gene mapping; DNA sequencing; restriction fragment length polymorphism (RFLP) analysis; and protein engineering.

Development: The design, development, simulation, or experimental testing of prototype or experimental hardware or systems to validate technological feasibility or concept of operation, to reduce technological risk and to provide test systems prior to production approval.

Establishment: A facility in which biotechnology is developed or utilized, or where biotechnology-related research and development takes place. Includes auxiliary facilities operated in conjunction with (whether or not physically separated from) such facilities.

Firm: An individual proprietorship, partnership, corporation (including any subsidiary corporation in which more than 50 percent of the outstanding voting stock is owned), cooperative, joint venture, consortium, association, business trust, trustees in bankruptcy, or receivers under decree of any court owning or controlling one or more establishments, as defined above.

Manufacturing Products: The output from manufacturing and production activities or associated with the concurrent development and maturation of the product design.

Research, Basic & Applied: Includes activities carried on by persons trained, either formally or by experience, in the biology or physical sciences including related engineering and software development, if the purpose of such activity is to do one or more of the following:

> **Basic Research:** Systematic study directed toward greater knowledge or understanding of the fundamental aspects of phenomena and of observable facts without specific applications towards processes or products in mind.
>
> **Applied Research:** Systematic study to gain knowledge or understanding necessary to determine the means by which a recognized and specific need may be met. It is a systematic application of knowledge toward the production of useful materials, devices and systems or methods, including design, development, and improvement of prototypes and new processes to meet specific requirements.

United States: Includes the fifty States, Puerto Rico, the District of Columbia, the Virgin Islands, American Samoa, and the Trust Territories of the Pacific Islands.

Note: Any information submitted in response to this survey will be deemed business confidential and exempt from public disclosure in accordance with section 705 of the Defense Production Act of 1950, as amended.

DEPARTMENT OF COMMERCE

BUSINESS CONFIDENTIAL

GENERAL INSTRUCTIONS

Who must complete this survey: Please complete this questionnaire if your company performs biotechnology research and development, uses a biotechnology process in manufacturing, or produces research tools. To determine if your firm is exempt from participating, please see page iv.

This survey has six sections as follows:

PART I – Firm Identification & Exemption

PART II – Biotechnology Activities

PART III – Human Resources

PART IV – Financial & Economic Conditions

PART V – Future Projections & Market Conditions

PART VI – Certification

1- **Multiple Business Units:** You must complete this survey for all of your U.S. biotechnology operations. You may combine all of the data from individual business units into one response, or submit separate surveys for each unit. When responding, please indicate how many surveys we should expect to receive from your firm.

2- **Estimates:** It is not our desire to impose any unreasonable burden on any respondent. If information requested is not available from your records in exactly the form indicated, furnish the most accurate estimates you are able to provide and designate these figures as such with the letter "E" following the estimate figure. If an item does not apply to your firm, please designate with the letters "N/A."

3- **Small Businesses**: Companies with fifty or fewer employees, please only provide one year of data as requested for questions 24, 25, 28, 29, 30 and 31.

4- **Questions** related to this survey should be faxed to (202) 482-5650 or directed to:
Robert Nichol, Senior Trade & Industry Analyst, (202) 482-1269, RNichol@bis.doc.gov
Mark Crawford, Senior Trade & Industry Analyst, (202) 482-8239, Mcrawfor@bis.doc.gov
Lee Ann Carpenter, Trade & Industry Analyst, (202) 482-2583, LCarpent@bis.doc.gov

5- If you are interested in downloading additional copies of the survey, please visit our website:
http://www.bis.doc.gov/OSIES/BioTechSurvey.doc (Microsoft Word)
http://www.bis.doc.gov/OSIES/BioTechSurvey.pdf (Adobe Acrobat)

6- **Before returning your completed survey**, be sure to: 1) sign the certification on page 17; 2) identify the name and phone number of the person(s) responsible for the completion and submission of this survey; and 3) make a copy of the completed survey for your records.

Please return the completed survey in the enclosed postage-paid envelope within 45 days of receipt to:

Mr. Brad Botwin, Division Director
BIS/SIES, Room 3876 B-1
U.S. Department of Commerce
14th Street & Constitution Avenue, NW
Washington, DC 20230

Note: Any information submitted in response to this survey will be deemed business confidential and exempt from public disclosure in accordance with section 705 of the Defense Production Act of 1950, as amended.

BUSINESS CONFIDENTIAL

FIRM IDENTIFICATION AND EXEMPTION

To determine whether your company is exempt from the requirement to complete this survey, first review the biotechnology definition on page ii. Second, if your company performs biotechnology research and development, uses a biotechnology process in manufacturing, or produces research tools, check the box of the major category from the list below that most accurately describes your company's *primary* (P) application of biotechnology and check the box(s) of all applicable *secondary* (S) applications of biotechnology. Finally, check the box(s) of subcategory(s) that most accurately describe your company's activity.

If you checked any category (1–8), then your firm is required to complete this survey.

Select the category(s) from the list below that most accurately describe your firm's area(s) of biotechnology activities.					
P	S		Utilizes human cells, genes, proteins, enzymes, antibodies, and/or other biological entities and components to prevent, diagnose, and fight infections and other diseases, as well as to correct genetic disorders.		
		1. Human health		**1.1.** Prevention	e.g., vaccines.
				1.2. Diagnostics	e.g., gene tagging, biosensors or polymerase chain reaction amplification.
				1.3. Therapeutics	e.g., biopharmaceuticals, gene therapy.
		2. Animal health	Creation of new vaccines, therapeutics, and other products to diagnose, treat and vaccinate animals for various diseases.		
		3. Agricultural & aquacultural/ marine	Utilizes or engineers biologically-derived products.		
				3.1. Seeds & plants	Better or more useful plants, crops or trees, and solutions to agricultural problems.
				3.2. Livestock	Better animal products, and solutions to livestock-related problems, excluding health-related.
				3.3. Aquaculture	Better aquatic plant and animal foods and byproducts.
		4. Marine & terrestrial microbial	Conducts research to determine potential uses for microorganisms.		
				4.1. Marine microbial	Explores the capabilities of marine microorganisms to develop new classes of human vaccines, medicines, and other medical products, chemical products, enzymes, and industrial processes.
				4.2. Terrestrial microbial	Explores the capabilities of terrestrial microorganisms such as extremophiles from geysers and volcanic vents.

(Table continued on next page)

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P	S				
		5. Industrial & Agricultural-derived processing	Applies the techniques of modern molecular biology to improve efficiency and reduce environmental impacts.		
				5.1. Specialty chemicals	e.g., amino acids, enzymes.
				5.2. Food processing	e.g., grain processing, bioprocessing (e.g., using enzymes and bacteria culture), vitamins, and phytochemicals (e.g., neutraceuticals or functional foods).
				5.3. Other chemicals & industrial activity	e.g., commodity chemicals, chemical feed stocks, fuels, lubricants, textiles, biopulping, biobleaching, paper, fuels, starch and grain processing, flavors & fragrances, plastics.
		6. Environmental remediation	Uses living organisms for a wide variety of applications in hazardous waste treatment and pollution prevention with regards to air, water, and soil (e.g., bioremediation, phytoremediation, biofiltration).		
		7. Natural resource recovery	Uses living organisms to facilitate the recovery or extraction of energy or minerals (e.g., microbiologically enhanced petroleum or mineral recovery, biodesulphurization).		
		8. Other	Describe: _____		
If your firm does not perform biotechnology research and development, use a biotechnology process in manufacturing, or produce research tools related to these areas (1–8), select category 9; your firm is exempt from completing this survey. Please complete the Certification Section (page 17) and return the entire survey to the address indicated on page iii.					
		9. No Biotechnology	This firm has not performed biotechnology research and development, used a biotechnology process in manufacturing, or produced research tools related to these biotechnology areas.		

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DEPARTMENT OF COMMERCE

BUSINESS CONFIDENTIAL

PART I – FIRM IDENTIFICATION

1) **U.S. BIOTECHNOLOGY AND/OR BIOTECHNOLOGY COMPONENT FIRM NAME AND ADDRESS**: Please provide your company name and address; year of firm establishment; your firm's DUNS number(1); and the NAICS code(2) for your firm's primary product.

_____
Firm Name

_____
Street Address

_____
City, State, Zip Code

_____ _____ _____
Year Established DUNS Number(1) Primary NAICS(2)

(1) To request a DUNS Number or to find the DUNS Number already assigned to your firm go to http://www.dnb.com/
(2) North American Industry Classification System (NAICS) Codes: http://www.census.gov/epcd/www/naics.html

2) **OWNERSHIP**: If your firm is wholly or partly owned by another firm, indicate the name and address of the parent firm, extent of ownership, and year acquired.

_____
Firm Name

_____
Street Address

_____
City, State, Zip Code (Country)

_____% _____
Ownership Year Acquired

3) Are the responses provided to this survey for more than one subsidiary or establishment of your firm engaged in biotechnology activities? Yes No

4) If yes, please identify the subsidiary(ies) or other establishments by listing their name and address as well as their DUNS number. (If more than two locations, please list them on the last page of this survey under "Comments.")

_____
Name, City, State, DUNS Number

_____
Name, City, State, DUNS Number

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PART II – BIOTECHNOLOGY ACTIVITIES

5) Indicate your firm's biotechnology activities. (Check all that apply.)

	Research	Development or Pre-clinical trials or Confined field tests Product	Development or Pre-clinical trials or Confined field tests Process	Clinical test or Unconfined Release Assessment	Approved, Marketed, or In production Products	Approved, Marketed, or In production Process
DNA-Based						
Gene Probes/DNA Markers	❑	❑	❑	❑	❑	❑
Bio-Informatics	❑	❑	❑	❑	❑	❑
Genomics/Pharmacogenetics	❑	❑	❑	❑	❑	❑
Genetic Engineering/DNA Sequencing/ Synthesis Amplification	❑	❑	❑	❑	❑	❑
Biochemistry/ Immunochemistry						
Vaccines/Immune Stimulants	❑	❑	❑	❑	❑	❑
Drug Design & Delivery	❑	❑	❑	❑	❑	❑
Diagnostic Tests/Antibiotics	❑	❑	❑	❑	❑	❑
Peptide/ Protein Sequencing/ Synthesis	❑	❑	❑	❑	❑	❑
Cell Receptors/Signaling Pheromones/ Structural Biology	❑	❑	❑	❑	❑	❑
Combinatorial Chemistry/3D Molecular Modeling	❑	❑	❑	❑	❑	❑
Biomaterials	❑	❑	❑	❑	❑	❑
Microbiology/Virology/ Microbial Ecology	❑	❑	❑	❑	❑	❑
Bioprocessing Based						
Cell/Tissue/Embryo Culture/Manipulation	❑	❑	❑	❑	❑	❑
Extraction/Purification/Separation	❑	❑	❑	❑	❑	❑
Fermentation/Bioprocessing/ Biotransformation/Natural Products	❑	❑	❑	❑	❑	❑
Chemistry	❑	❑	❑	❑	❑	❑
Environment						
Bioleaching/Biopulping/Biobleaching/ Biodesulphurization	❑	❑	❑	❑	❑	❑
Bioremediation/Biofiltration	❑	❑	❑	❑	❑	❑
Other (Specify):						
	❑	❑	❑	❑	❑	❑

6) A. Please briefly describe your firm's in-house biotechnology capabilities and operations (research, production, tools).

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B. Please briefly describe capabilities and operations (research, production, tools) that your firm contracts out.

_____

_____

_____

_____

_____

_____

7) Is biotechnology central to your **(firm or division)**? ❑ Yes ❑ No

8) Are your current physical facilities adequate to serve your expected infrastructure needs for the next two years? ❑ Yes ❑ No

9) Is your firm contemplating (check all that apply)

❑ expanding facilities/infrastructure (including lease)?

❑ contracting work out to other U.S. firms/facilities?

❑ contracting work out to non-U.S. firms/facilities?

Please explain your answer. _____

_____

10) If your firm has a Bio Safety Level certified facility, what is the level of certification?

❑ Level 1 ❑ Level 2 ❑ Level 3 ❑ Level 4

11) Does your firm plan to construct a Level 3 or 4 Bio Safety Level certified facility within the next three years? ❑ Yes ❑ No

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PART III – HUMAN RESOURCES

12) How many full-time equivalent, in-house people does your **firm or division** currently employ **in the U.S.**? (Include temporary vacancies.) _____

13) How many full-time equivalent U.S. employees have biotechnology-related responsibilities? _____

14) For both in-house and contract **employees that have biotechnology-related responsibilities**, state the number of full-time employees or full-time equivalents (*35–40 hours/week for a full twelve months or working full-time on biotechnology equal to or more than 50% of time*) by occupation.

Occupation	2000			2001			2002 (est)		
	In-House	Contract Out		In-House	Contract Out		In-House	Contract Out	
		D	F		D	F		D	F
Biotechnology R&D Activities									
Scientists									
Engineers									
Science and Clinical Laboratory Technicians									
R & D focused Computer Specialists									
Biotechnology Administration & Production									
General Operations, Marketing & Financial Managers									
Legal (e.g., intellectual property & regulatory issues)									
Production Managers and Supervisors									
Production or Agri/Aquacultural workers									

D = Contract out to **U.S. located** firms
F = Contract out to **Foreign located** firms

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15) Does your firm currently have any full-time biotechnology-related positions that have been unfilled for more than three months?

If **Yes**, please indicate the number of unfilled positions in the following categories and identify the reason that the position is presently unfilled.

If **None**, check No and proceed to the next question. ❑ No

Occupation	Number of Positions Unfilled for more than 3 months	Reason
Biotechnology Research and Development Activities		
Scientists		
Engineers		
Science and Clinical Laboratory Technicians		
R & D focused Computer Specialists		
Biotechnology Administration & Production		
General, Operations, Marketing, and Financial Managers		
Legal (e.g., intellectual property and regulatory issues)		
Production Managers or Supervisors		
Production or Agri/ Aquacultural workers		

16) What is your average annual employee turnover rate for employees with primarily biotechnology-related responsibilities? _____ %

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17) Please identify the percentage (%) of your firm's biotechnology work force that is obtained from the following sources (because categories may overlap, percentages need not add up to 100%).

Recruited from the local labor market/U.S. firms _____%

Recruited from U.S. 4-year degree or post-graduate degree granting colleges/universities _____%

Recruited from U.S. 2-year community or junior colleges, or technical schools _____%

Foreign employees with a U.S. visa or work permit _____%

Foreign employees residing abroad _____%

18) Please estimate the percentage (%) of your workforce needs that are fulfilled by the following:

Contracting out to other U.S. headquartered firms _____%

Contracting out to foreign firms operating abroad _____%

Contracting out to a U.S. university, college, or nonprofit organization _____%

19) Please indicate all occupations that will be the focus of your company's recruiting efforts in the next **three** years (replacement hires and new positions):

Biotechnology Research and Development Activities	
Scientists	❑
Engineers	❑
Science and Clinical Laboratory Technicians	❑
R & D focused Computer Specialists	❑
Biotechnology Administration and Production	
General Operations, Marketing and Financial Managers	❑
Legal (e.g., intellectual property and regulatory issues)	❑
Production Managers and Supervisors	❑
Production or Agri/Aquacultural workers	❑

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20) What steps are you taking or contemplating to ensure a sufficient number of adequately skilled workers and professionals for your firm?

❏ In-house training
❏ College recruiting
❏ Increase salaries
❏ Overtime incentives
❏ Foreign recruiting
❏ Establish foreign facilities to gain access to more workers
❏ Recruiting bonuses
❏ Enhanced benefit plans
❏ Subcontract to another company or academia
❏ Outsourcing
❏ Other (Specify) _____

21) If your firm's U.S. operations recruit workers from abroad, list the top four countries that provide a source of employees.

1.

2.

3.

4.

22) Does your firm expect to become more dependent on foreign nationals working on temporary visas or work permits within the next **three** years? ❏ Yes ❏ No

23) What percentage of your work force requires security clearances to perform work for U.S. Government Departments or Agencies? _____%

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BUSINESS CONFIDENTIAL

PART IV - FINANCIAL AND ECONOMIC CONDITIONS

24) Please provide ***Financial Data*** as specified for the fiscal years below:*
(in $000s: e.g., $25,000 = $25).

Category	2000 ($000s)	2001 ($000s)	2002 (est) ($000s)	2003 (est) ($000s)
For Entire Business (i.e., biotechnology and non-biotechnology)				
Net Sales				
Cost of Goods Sold				
Selling, General, and Administrative Expenses				
Operating Income (line 1 minus lines (2+3)				
FOR BIOTECHNOLOGY ONLY				
Net Sales				
Cost of Goods Sold				
Selling, General, and Administrative Expenses				
Operating Income (line 1 minus lines (2+3)				

*** Companies with 50 employees or less are only required to provide 2001 data**

25) Please provide ***Research and Development Expenditures*** as specified for the years below:*
(in $000s: e.g., $25,000 = $25)

Category	2000 ($000s)	2001 ($000s)	2002 (est) ($000s)	2003 (est) ($000s)
For Entire Business (i.e., biotechnology and non-biotechnology)				
Research				
Development				
Total R&D				
FOR BIOTECHNOLOGY ONLY				
Research				
Development				
Total R&D				

*** Companies with 50 employees or less are only required to provide 2001 data**

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26) If your firm works with any federal agency in any of the following ways as part of your biotechnology activities, please indicate the agency. See the boxes at the bottom of the table for definitions of abbreviations.

Programs	Agency (s)			
Grants Programs ❑ SBIR ❑ STTR ❑ Other Grants	❑ ARS ❑ CDC ❑ DoD ❑ DoE ❑ DoJ	❑ DoS ❑ DoT ❑ EPA ❑ FDA ❑ HHS	❑ NASA ❑ NIH ❑ NIST ❑ NOAA ❑ NSF	❑ SBA ❑ USDA ❑ VA ❑ Other _____
❑ Technical Assistance Programs (BMP, MEP...)	❑ ARS ❑ CDC ❑ DoD ❑ DoE ❑ DoJ	❑ DoS ❑ DoT ❑ EPA ❑ FDA ❑ HHS	❑ NASA ❑ NIH ❑ NIST ❑ NOAA ❑ NSF	❑ SBA ❑ USDA ❑ VA ❑ Other _____
❑ Government Loan Programs	❑ ARS ❑ CDC ❑ DoD ❑ DoE ❑ DoJ	❑ DoS ❑ DoT ❑ EPA ❑ FDA ❑ HHS	❑ NASA ❑ NIH ❑ NIST ❑ NOAA ❑ NSF	❑ SBA ❑ USDA ❑ VA ❑ Other _____
❑ Contracts (including ACTD, ATD, SBIR & STTR) ❑ CRADA ❑ In-Licensing	❑ ARS ❑ CDC ❑ DoD ❑ DoE ❑ DoJ	❑ DoS ❑ DoT ❑ EPA ❑ FDA ❑ HHS	❑ NASA ❑ NIH ❑ NIST ❑ NOAA ❑ NSF	❑ SBA ❑ USDA ❑ VA ❑ Other _____
❑ "Work-for-others" done at federal laboratories ❑ Other (specify) _____	❑ ARS ❑ CDC ❑ DoD ❑ DoE ❑ DoJ	❑ DoS ❑ DoT ❑ EPA ❑ FDA ❑ HHS	❑ NASA ❑ NIH ❑ NIST ❑ NOAA ❑ NSF	❑ SBA ❑ USDA ❑ VA ❑ Other _____

Programs:

ACTD=Advanced Concept Technology Demonstration;

ATD=Advanced Technology Demonstration;

BMP=Best Manufacturing Practices;

CRADA=Cooperative Research and Development Agreement;

MANTECH=Manufacturing Technology;

MEP=Manufacturing Extension Program;

SBIR=Small Business Innovation Research;

STTR=Small Business Technology Transfer

Agencies: (not all-inclusive)

ARS=Agriculture Research Service;

CDC=Centers for Disease Control;

DoD=Department of Defense;

DoE= Department of Energy;

DoJ=Department of Justice, including the FBI (Federal Bureau of Investigation);

DoS=Department of State;

DoT=Department of Treasury;

EPA=Environmental Protection Agency;

FDA=Food and Drug Administration

HHS=Department of Health and Human Services;

NASA=National Aeronautics & Space Administration;

NIH=National Institutes of Health;

NIST=National Institute of Standards & Technology;

NOAA=National Oceanic and Atmospheric Administration;

NSF=National Science Foundation;

SBA=Small Business Administration;

USDA= Department of Agriculture;

VA=Veterans Administration

Note: Any information submitted in response to this survey will be deemed business confidential and exempt from public disclosure in accordance with section 705 of the Defense Production Act of 1950, as amended.

BUSINESS CONFIDENTIAL

27) Has your firm ever competed for a federal government contract? ❑ Yes ❑ No

In the context of your firm's response **(<u>either yes or no</u>)**, what parts of Government contracting does your firm find challenging? (select all that apply):

❑ Unable to locate proper Government contract or agency for business

❑ Length of term on Government contracts is too long

❑ Length of term on Government contracts is too short

❑ Uncertainty of Government demand

❑ Billing/Payment complications

❑ Lack of balanced overall delivery schedules

❑ Meeting the regulatory and/or performance requirements for a contract award or product approval/acceptance

❑ Other (specify) _____

28) Provide **Capital Expenditures** as specified for the fiscal years below:* (in $000s: e.g., $25,000 = $25).

Category	2000 ($000s)	2001 ($000s)	2002 (est) ($000s)	2003 (est) ($000s)
For Entire Business (i.e., biotechnology and non-biotechnology)				
New Plant and Facilities				
New Machinery and Equipment				
Total Capital Expenditures				
FOR BIOTECHNOLOGY ONLY				
New Plant and Facilities				
New Machinery and Equipment				
Total Capital Expenditures				

* **Companies with 50 employees or less are only required to provide 2001 data**

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BUSINESS CONFIDENTIAL

29) **Biotechnology Research and Development** - Provide the **total amount** expended (*or that is projected to be spent*) by your firm on biotechnology research and development for *business fiscal years* 2000 through 2003 (in $000s: $25=$25,000). *

Year	2000 Total ($000s)	2001 Total ($000s)	2002 Total (est) ($000s)	2003 Total (est) ($000s)
Biotechnology R&D Expenditures				

Identify **the percentage** of your total R&D budget (as reported above) that individual sources represent in each year.*

Funding Sources	2000 %	2001 %	2002 (est) %	2003 (est) %
In-House Revenue				
Parent Firm Funding				
Conventional Loans				
Angel Investors				
Venture Capital Firms				
Initial Public Offering				
U.S. Gov't Loan/Grant				
State Gov't Loan/Grant				
Foreign Gov't Loan/Grant				
Private Research Grants				
Other (specify)				
Other (specify)				
Total	**100%**	**100%**	**100%**	**100%**

***Companies with 50 employees or less are only required to provide 2001 data.**

30) **Exports**: What percent of your net revenues are generated from exports of biotechnology products or processes by fiscal year (2000–2003)*?

Year	2000	2001	2002 (est)	2003 (est)
Percent of Net Revenue	%	%	%	%

***Companies with 50 employees or less are only required to provide 2001 data.**

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BUSINESS CONFIDENTIAL

31) For the years your firm exported biotechnology products or processes, please provide a percentage breakout of your export revenues by geographic location.*

Location	2000	2001	2002 (est)	2003 (est)
Canada	%	%	%	%
Mexico	%	%	%	%
Brazil				
Other Latin America				
UK	%	%	%	%
Germany				
France				
Russia				
Other EU				
Australia	%	%	%	%
India				
Israel				
Korea				
Japan				
China				
Other Asia				
Other (Specify)	%	%	%	%
Total	**100%**	**100%**	**100%**	**100%**

*** Companies with fewer than 50 employees are only required to complete 2001 data**

Note: Any information submitted in response to this survey will be deemed business confidential and exempt from public disclosure in accordance with section 705 of the Defense Production Act of 1950, as amended.

BUSINESS CONFIDENTIAL

PART V – FUTURE PROJECTIONS & MARKET CONDITIONS

32) Which of the following strategies does your firm plan to use in 2002-2003? (**Check all that apply**)

- ❑ Refocus product development
- ❑ Refocus R&D activities
- ❑ Downsize operations
- ❑ Expand operations
- ❑ Enter product trials
- ❑ Launch new product
- ❑ Acquire a company
- ❑ Recruit employees from abroad
- ❑ Increase recruitment efforts for U.S. workers
- ❑ License-in technology
- ❑ License-out technology
- ❑ Merge with other company
- ❑ Form a joint venture
- ❑ Expand into foreign markets
- ❑ Outsource production
- ❑ Establish facilities abroad
- ❑ No change
- ❑ Other (Specify) _____

33) Which of the following selections best describes the competitive prospects for your business operations in the next two years?

- ❑ Improve greatly
- ❑ Improve somewhat
- ❑ Remain stable
- ❑ Decline somewhat
- ❑ Decline greatly

34) How many United States Patent and Trademark Office *current biotechnology patents or patents pending* does your firm have? (Indicate zero if none)

Current: _____ Pending: _____

Note: Any information submitted in response to this survey will be deemed business confidential and exempt from public disclosure in accordance with section 705 of the Defense Production Act of 1950, as amended.

BUSINESS CONFIDENTIAL

35) During 2000–2001, did your firm grant the right to use intellectual property to another firm or did your firm acquire the right to use intellectual property from another firm? If "**Yes**," please indicate the type and direction of such intellectual property transfer:

	Granted Rights to *Domestic* Firms	**Acquired Rights from *Domestic* Firms**	**Granted Rights to *Foreign* Firms**	**Acquired Rights from *Foreign* Firms**
Intellectual Property	**Yes**	**Yes**	**Yes**	**Yes**
Trade Secrets	❑	❑	❑	❑
Patents	❑	❑	❑	❑
Plant Breeders' Rights	❑	❑	❑	❑
Other (Specify)	❑	❑	❑	❑

36) List the countries of your top three *foreign competitors*.

1. _____

2. _____

3. _____

Note: Any information submitted in response to this survey will be deemed business confidential and exempt from public disclosure in accordance with section 705 of the Defense Production Act of 1950, as amended.

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37) Identify the barriers from the list below that impede your firm's advancement of biotechnology research or product commercialization. For those impediments, describe the degree of difficulty for that barrier, with 1 being no barrier and 5 being a high barrier.

Barrier	**1**	**2**	**3**	**4**	**5**
Access to start-up capital					
Access to technology					
Access to information					
Size of market					
Unfair foreign laws					
Unfair U.S. laws					
Access to international market					
Export control regulations					
Import regulations					
Lack of qualified biotechnology employees					
Distribution and transportation costs					
Marketing costs					
Research costs					
Shortage of approved U.S. manufacturing facilities					
Patent fees and approval process					
Patent rights held by third parties					
Lack of patent protection abroad for product/process					
Lack of understanding or interest by U.S. gov't. policymakers					
Antiquated rules and regulations					
Transportation regulations (including hazardous material handling regulations)					
Regulatory approval process and costs					
Antitrust laws					
Liability concerns/Insurance costs					
Unfair competition					
Government procurement practices/regulations					
Equipment shortage					
Insufficient or unstable government funding for R&D					
Construction delays					
Public acceptance/Ethical considerations					
Local zoning and permitting practices					
Other (Specify)					

Note: Any information submitted in response to this survey will be deemed business confidential and exempt from public disclosure in accordance with section 705 of the Defense Production Act of 1950, as amended.

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38) What additional actions, policy changes, regulatory reforms, or assistance could the Federal Government take to help your firm improve competitiveness?

_____

_____

_____

_____

39) Has your firm had a defense contract, as a prime or sub-contractor, within the last five years? If No, proceed to 45. ❑ Yes ❑ No

40) If yes, does your firm sell this product to the Department of Defense as a commercial or non-developmental item? ❑ Yes ❑ No

41) Does your firm currently have a defense contract? ❑ Yes ❑ No

If your firm provides products directly to the Department of Defense:

42) Is the product sold at catalog pricing (i.e., from a published price list)? ❑ Yes ❑ No

43) Is the value added of the product(s) performed by the same employees, same facilities, and same equipment as any product provided to commercial customers? ❑ Yes ❑ No

44) If applicable, is the production lead-time quoted the same as quoted to your commercial customers? ❑ Yes ❑ No

45) Is your business registered in the Central Contractor Registration? See http://www.ccr.gov/ ❑ Yes ❑ No

46) In the last five years has your firm exited the defense market? ❑ Yes ❑ No

If **yes**, for which of the following reasons? (select all that apply)

❑ Inconsistent procurement practices

❑ Decrease in defense demand

❑ Department of Defense regulations too cumbersome

❑ Sold defense portion of business

❑ Merger/Acquisition

❑ Commercial market more profitable

❑ Delays in payment

❑ Onerous compliance with the Federal Acquisition Regulations

❑ Other (specify)

Note: Any information submitted in response to this survey will be deemed business confidential and exempt from public disclosure in accordance with section 705 of the Defense Production Act of 1950, as amended.

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PART VI – Certification

The undersigned certifies that the information herein supplied in response to this questionnaire is complete and correct to the best of his/her knowledge. It is a criminal offense to willfully make a false statement or representation to any department or agency of the United States Government as to any matter within its jurisdiction. (18 U.S.C.A. 1001 (1984 & SUPP. 1197))

Company Name

Authorizing Official – Print Name

Title | Phone Number | Ext.

Signature | Date

Point of Contact- Print Name | Title

Email | Phone Number | Ext.

If you would like a copy of the final biotechnology assessment, please check the box: ❑

Comments (optional): In the space below, provide any additional comments or any other information you wish to include regarding your biotechnology operations or other related issues that impact your firm. In addition, what industry needs and concerns did this survey fail to address?

Note: Any information submitted in response to this survey will be deemed business confidential and exempt from public disclosure in accordance with section 705 of the Defense Production Act of 1950, as amended.

Appendix B
Growth Rate Methodology

Share-Weighted Growth Rate Methodology—Chapter 4

A share-weighted growth rate of an aggregate takes into account size differences of components (respondents), whereas an unweighted growth rate is based on a simple average of respondents, or total. The following discussion demonstrates how a share-weighted growth rate is calculated.

The growth rate of an aggregate or sum is influenced by the share and growth rate of an individual respondent. This is shown below.

Let i denote one respondent among a total of N, i.e., $i = 1, ..., N$. Let there be two time-periods t–1 and t. Denote the value of a variable of the ith respondent in these two periods by $X_{i,t-1}$ and $X_{i,t}$. Also, denote the corresponding sums of all respondents by S_{t-1} and S_t. Therefore, by definition,

$$S_{t-1} = X_{1,t-1} + X_{2,t-1} + \Lambda + X_{N,t-1} \tag{1}$$

and

$$S_t = X_{1,t} + X_{2,t} + \Lambda + X_{N,t} \, . \tag{2}$$

Hence, the growth rate G of S_{t-1} to S_t is,

$$G = \frac{S_t - S_{t-1}}{S_{t-1}} \, . \tag{3}$$

Combining (1), (2), and (3),

$$G = \frac{X_{1,t} - X_{1,t-1}}{S_{t-1}} + \frac{X_{2,t} - X_{2,t-1}}{S_{t-1}} + \Lambda + \frac{X_{N,t} - X_{N,t-1}}{S_{t-1}} \, . \tag{4}$$

Finally, equation (4) can be rewritten to express G as the share-weighted sum of the growth rates of the individual respondents. This is given by,

$$G = \left(\frac{X_{1,t-1}}{S_{t-1}}\right)\left(\frac{X_{1,t} - X_{1,t-1}}{X_{1,t-1}}\right) + \left(\frac{X_{2,t-1}}{S_{t-1}}\right)\left(\frac{X_{2,t} - X_{2,t-1}}{X_{2,t-1}}\right) + \Lambda + \left(\frac{X_{N,t-1}}{S_{t-1}}\right)\left(\frac{X_{N,t} - X_{N,t-1}}{X_{N,t-1}}\right) \, . \tag{5}$$

Notice that the right-hand side of (5) consists of similar terms being summed. In this case, each term equals the *respondent's share* in the preceding period sum, S_{t-1}, *multiplied* by the *respondent's growth rate* from the preceding period, t–1, to the next period, t. That is, equation (5) states that the aggregate growth rate, G, is the share-weighted sum of the growth rates of all respondents. This equation was used in the analysis for Chapter 4 on the economic performance of firms.

It is important to note that equation (3) and equation (5) will yield the same aggregate growth rate, *G*, if the sum in (1) and the sum in (2) have exactly the same number of non-zero observations. That is, if an observation is a value provided by a respondent, each respondent must provide a non-zero value in each period. Otherwise, equations (3) and (5) will yield different values of the aggregate growth rate, *G*.

To see the above situation, suppose that respondent 1 provides in period t–1 a zero value, i.e., $X_{1,t-1} = 0$, but provides in period t a value, $X_{1,t}$, that is non-zero. In this example, respondent 1 will be *completely eliminated* by equation (5) because the first term on the right hand side for respondent 1 equals zero, so that even the non-zero value of $X_{1,t}$ is also eliminated in the computation of *G*.

Contrast the above with equation (3). Since $X_{1,t-1} = 0$, respondent 1 is not included in equation (1). However, because $X_{1,t}$ is non-zero, respondent 1 is included in equation (2). Therefore, respondent 1 is *partly included* by equation (3) in the computation of *G*.

It should be noted that survey respondents with 50 employees or fewer were required to provide data only for 2001. Only a small number of these companies provided annual data that could be used in growth rate calculations. Therefore, calculated growth rates primarily reflect growth rates for the larger companies in the survey population.

Annual Growth Rate Methodology—Chapter 6

Annual growth rates, r, for employment, as reported in Chapter 6, were calculated using the following equation:

$$r = [(X_1/X_0)^{(1/n)}]-1,$$

where X_1 is employment in 2002, X_0 is employment in 2000, and n is the number of years, or 2, in this case.

Note that the growth rates in Chapter 6 were based on a panel of 850 firms that responded to *CTA,* question 14 for all three years.

APPENDIX C
DATA TABLES

Referred to in Chapter 2

Table C.1 Funding Sources by Firm Size, Year 2000 through 2003

Referred to in Chapter 3

Table C.2 Number of Firms per Primary Biotechnology Application by NAICS Code Category

Corresponding to each of the application categories discussed in Chapter 3

Table C.3a Economic and Business Statistics, Averages by Company Size, Respondents Working in Human Health Applications, 2001

Table C.3b Economic and Business Statistics, Averages by Company Size, Respondents Working in Agriculture and Aquaculture/Marine Applications, 2001

Table C.3c Economic and Business Statistics, Averages by Company Size, Respondents Working in Animal Health Applications, 2001

Table C.3d Economic and Business Statistics, Averages by Company Size, Respondents Working in Industrial and Agriculture-derived Processing Applications, 2001

Table C.3e Economic and Business Statistics, Averages by Company Size, Respondents Working in Marine and Terrestrial Microbial Applications, 2001

Table C.3f Economic and Business Statistics, Averages by Company Size, Respondents Working in Environmental Remediation and Natural Resource Recovery Applications, 2001

Table C.3g Economic and Business Statistics, Averages by Company Size, Respondents Working in "Other" Applications, 2001

Table C.1: Funding Sources by Firm Size, Year 2000 through 2003

Firm Size Sort	Firm Size	Fiscal Year	# of Firms	In-House Revenue	Parent Firm Funding	Conventional Loans	Angel Investors	Venture Capital Firms	Initial Public Offering	U.S. Gov't Loan/Grant	State Gov't Loan/Grant	Foreign Gov't Loan/Grant	Private Research Grants
1	>1 and <10.5	FY 2000	55	20	1	1	21	9	1	11	2	0	0
2	≥10.5 and <50.5	FY 2000	86	37	6	1	18	22	3	9	1	1	2
3	≥50.5 and <500.5	FY 2000	290	167	30	13	16	68	27	57	7	5	12
4	≥500.5 and <2,500.5	FY 2000	50	44	6	1	0	1	1	8	2	1	3
5	≥2,500.5 and <14,999.5	FY 2000	28	24	6	0	0	0	1	2	2	0	1
6	>14,999.5	FY 2000	17	13	4	0	0	0	0	4	0	0	2
	Total		526	305	53	16	55	100	33	91	14	7	20
1	>1 and <10.5	FY 2001	217	114	10	11	53	29	2	61	5	1	9
2	≥10.5 and <50.5	FY 2001	308	143	20	14	66	97	5	71	13	1	13
3	≥50.5 and <500.5	FY 2001	296	174	30	17	13	65	33	65	8	5	15
4	≥500.5 and <2,500.5	FY 2001	51	44	7	1	0	1	1	8	2	1	3
5	≥2,500.5 and <14,999.5	FY 2001	30	26	6	0	0	0	0	2	2	0	1
6	>14,999.5	FY 2001	19	14	5	0	0	0	0	4	0	0	2
	Total		921	515	78	43	132	192	41	211	30	8	43
1	>1 and <10.5	FY 2002	83	39	3	5	24	15	3	24	4	1	5
2	≥10.5 and <50.5	FY 2002	105	48	10	7	21	39	4	19	2	0	2
3	≥50.5 and <500.5	FY 2002	292	184	33	14	10	59	28	60	7	3	13
4	≥500.5 and <2,500.5	FY 2002	51	42	8	1	0	0	1	9	3	2	3
5	≥2,500.5 and <14,999.5	FY 2002	27	23	6	0	0	0	0	2	2	0	1
6	>14,999.5	FY 2002	17	12	5	0	0	0	0	4	0	0	2
	Total		575	348	65	27	55	113	36	118	18	6	26
1	>1 and <10.5	FY 2003	76	40	2	4	16	22	4	24	4	2	8
2	≥10.5 and <50.5	FY 2003	90	46	8	6	12	40	5	22	1	0	2
3	≥50.5 and <500.5	FY 2003	271	176	33	10	7	45	27	57	6	4	12
4	≥500.5 and <2,500.5	FY 2003	47	40	6	1	0	0	1	8	2	2	5
5	≥2,500.5 and <14,999.5	FY 2003	25	21	6	0	0	0	0	2	1	0	1
6	>14,999.5	FY 2003	17	13	5	0	0	0	0	4	0	0	2
	Total		526	336	60	21	35	107	37	117	14	8	30

Care should be exercised in making annual comparisons because funding sources from one year may carry into subsequent years as, for example, when a firm receives a multi-year grant. Also, firms with 50 or fewer employees were required to provide data only for 2001.

Table C.2: Number of Firms per Primary Biotechnology Application by NAICS Code Category

				Number of firms per primary biotech application						
Major sector	Detailed industry	NAICS Code	Total number of biotech firms per NAICS code	Human health	Animal health	Agriculture & aquacultural/ marine	Marine & terrestrial microbial	Industrial & agriculture-derived processing	Environmental & natural resources	Other
Basic industries & materials	Agriculture, forestry, fishing & hunting	111	2	0	0	2	0	0	0	0
		111211	2	0	0	2	0	0	0	0
		112930	1	1	1	0	0	0	0	0
		113	1	0	0	1	0	0	0	0
		1151	2	0	0	2	0	0	0	0
		11521	2	0	0	2	0	0	0	0
		11998	1	0	0	0	0	1	0	0
	Food, beverage, tobacco manufacture	311111	1	0	0	0	0	1	0	0
		311119	2	0	0	2	0	1	0	0
		3112	1	0	0	0	0	1	0	0
		311221	1	0	0	1	0	1	0	0
		311225	1	0	0	1	0	0	0	0
		31123	1	0	0	0	0	1	0	0
		3115	1	0	0	0	0	1	0	0
		3119	2	1	0	1	0	0	0	0
		311900	1	0	0	0	0	1	0	0
		311999	2	0	0	0	0	2	0	0
		31212	1	0	0	0	0	1	0	0
		31212	1	0	0	0	0	1	0	0
		312221	1	0	0	1	0	0	0	0
	Paper & wood manufacture	322121	1	1	0	0	0	0	0	0
	Petroleum & coal products manufacture	32411	1	0	0	0	0	0	1	1
	Plastics & rubber products manufacture	326	1	0	0	0	0	0	0	1
		32619	1	1	1	0	0	1	0	0
	Furniture & laboratory apparatus manufacture	339	5	4	0	0	0	0	1	0
		339111	2	2	0	0	0	0	0	0
	Other basic industries activity	2321	1	0	1	0	0	0	0	0
		32791	1	1	0	0	0	0	0	0
		3399	3	2	0	0	0	0	0	2

Table C.2: Number of Firms per Primary Biotechnology Application by NAICS Code Category

				Number of firms per primary biotech application						
Major sector	Detailed industry	NAICS Code	Total number of biotech firms per NAICS code	Human health	Animal health	Agriculture & aquacultural/ marine	Marine & terrestrial microbial	Industrial & agriculture-derived processing	Environmental & natural resources	Other
Chemical manufacture	Basic chemical manufacture	3251	7	3	0	0	0	2	1	1
		32513	1	0	0	1	0	0	0	0
		325188	1	0	0	0	0	0	0	1
		325199	10	5	0	0	1	3	0	2
	Resin, synthetic rubber & fibers manufacture	325211	2	0	0	1	0	1	0	0
	Agricultural chemical manufacture	3253	3	0	0	2	1	0	1	0
		32531	2	0	0	1	0	0	1	0
		32532	3	0	1	3	0	0	0	0
	Paint, coatings, adhesives, cleaning, surface agent manufacture	32562	1	0	0	0	0	1	0	
	All other chemical product manufacture	325	8	6	1	1	0	3	0	1
		325998	7	1	1	0	0	2	0	3
Information & electronics manufacture & services	Computer peripheral equipment & terminal manufacture	334119	1	0	0	0	0	0	0	1
	Semiconductor & related device manufacture	334413	1	1	0	0	0	0	0	0
	Instrument manufacture	3345	2	1	0	0	0	0	0	1
		334516	29	17	1	1	0	1	1	12
		334519	2	0	0	0	0	0	0	2
	Electrical equipment, appliance & component manufacture	335999	1	0	0	0	0	0	0	1
	Software publishers	51121	5	0	0	0	0	0	0	5
	Motion picture & sound recording industries	5122	1	1	1	0	0	0	0	0
	Computer systems design & related services	5415	1	0	0	0	0	0	0	1
		541519	1	0	0	0	0	0	0	1

Table C.2: Number of Firms per Primary Biotechnology Application by NAICS Code Category

				Number of firms per primary biotech application						
Major sector	Detailed industry	NAICS Code	Total number of biotech firms per NAICS code	Human health	Animal health	Agriculture & aquacultural/ marine	Marine & terrestrial microbial	Industrial & agriculture-derived processing	Environmental & natural resources	Other
Machinery manufacture	Commercial & service industry machinery manufacture	333319	1	0	0	0	0	0	1	0
	Other industrial machinery manufacture	333298	2	0	0	0	0	0	1	1
		333411	2	1	0	0	0	0	1	1
		333513	1	1	0	0	0	0	0	0
Medical substances & devices	Pharmaceutical & medicine manufacture	3254	27	23	3	0	0	0	0	2
		32541	24	19	1	0	1	1	0	2
		325412	66	60	5	0	0	2	0	2
	Medicinal & botanical manufacture	325411	7	5	0	0	0	1	0	1
	In-vitro diagnostic substance manufacture	325413	50	42	4	2	1	2	0	4
	Non-diagnostic biological product manufacture	325414	127	84	6	10	0	4	4	23
	Medical instruments, equipment & supplies manufacture	33451	2	2	0	0	0	0	0	0
		3391	3	3	0	0	0	0	0	0
		33911	4	3	0	0	0	0	0	1
		339112	20	18	0	1	0	0	0	1
		339113	7	6	0	0	0	0	0	1
Various services	Wholesale & retail, transport & warehousing	42145	1	1	0	0	0	0	0	0
		4222	1	1	0	0	0	0	0	0
		42221	2	2	0	0	0	0	0	0
		4226	1	1	0	0	0	0	0	1
		42269	1	0	0	0	0	1	0	0
		42291	1	0	0	0	0	1	0	0
		42345	1	1	0	0	0	0	0	0
		42349	1	0	0	0	0	0	0	1
		42491	5	3	0	2	0	0	0	0
		44612	1	0	0	0	0	0	0	1

Table C.2: Number of Firms per Primary Biotechnology Application by NAICS Code Category

				Number of firms per primary biotech application						
Major sector	Detailed industry	NAICS Code	Total number of biotech firms per NAICS code	Human health	Animal health	Agriculture & aquacultural/ marine	Marine & terrestrial microbial	Industrial & agriculture-derived processing	Environmental natural resources	Other
Various services, cont.	Profes., scientific, & technical services	54	1	1	0	0	0	0	0	0
	except computer & sci. R&D serv.	54108	1	1	0	0	0	0	0	0
		54133	5	4	0	0	0	0	0	1
		5416	2	2	0	0	0	0	0	0
		54161	5	2	1	0	0	0	2	0
		54162	1	0	0	0	1	0	1	0
		54169	4	3	0	0	0	0	1	0
		5419	1	0	0	0	0	0	0	1
		54199	2	2	0	0	0	0	0	0
		5471	1	1	0	0	0	0	0	0
	Testing laboratories	54138	20	9	0	1	0	2	2	7
	Scientific R&D services	5417	30	27	1	1	0	2	0	1
		54171	299	250	7	12	6	15	3	32
		54172	3	2	0	0	0	0	0	2
		54174	1	1	0	0	0	0	0	0
	Management of companies &	551112	3	1	0	0	1	1	0	1
	enterprises	551114	3	2	0	1	0	0	0	0
	Admin., support, waste management & remediation services	56291	1	0	0	0	0	0	1	0
	Other services	62	1	1	0	0	0	0	0	0
		621991	1	1	0	0	0	0	0	0
		62211	1	1	0	0	0	0	0	0
		62419	1	1	0	0	0	0	0	0
	Medical & diagnostic laboratories	6215	2	2	0	0	0	0	0	0
		62151	6	6	0	0	0	0	0	0
		621511	9	7	0	0	0	0	0	2
		621512	3	3	0	0	0	0	0	0
NAICS code not reported		NR	134	93	5	15	3	11	4	19
Total number of firms			**1031**	**747**	**41**	**70**	**15**	**69**	**27**	**144**

Table C.3a: Economic and Business Statistics, Averages by Company Size, Respondents Working in Human Health Applications, 2001

	Number of companies*	Employees ** Avg. (FTEs)	Net Sales Avg. ($ thousand)	Operating Income Avg. ($ thousand)	Capital Expenditures Avg. ($ thousand)	R&D Expenditures Avg. ($ thousand)
All companies reporting	780					
Entire business		1,094	$600,756	$115,587	$31,776	$54,511
Biotech activities		151	$65,326	$12,876	$8,368	$21,612
Segment: > 15,000 employees	14					
Entire business		42,708	$26,437,629	$4,646,172	$1,080,343	$1,150,298
Biotech activities		1,450	$1,251,432	$412,623	$154,233	$247,686
Segment: 2,501–15,000 employees	23					
Entire business		6,688	$4,233,405	$1,234,379	$247,506	$638,847
Biotech activities		1,620	$734,136	$194,368	$66,939	$164,328
Segment: 501–2,500 employees	42					
Entire business		1,272	$523,485	$95,364	$36,076	$110,448
Biotech activities		638	$235,800	$51,978	$26,536	$88,940
Segment: 51–500 employees	245					
Entire business		159	$22,393	–$5,901	$5,278	$19,213
Biotech activities		110	$17,225	–$7,068	$4,799	$18,430
Segment: 11–50 employees	264					
Entire business		26	$2,177	–$1,843	$1,103	$3,389
Biotech activities		20	$1,389	–$1,887	$1,035	$3,277
Segment: 1–10 employees	186					
Entire business		5	$2,006	–$684	$554	$918
Biotech activities		4	$2,080	–$656	$67	$914

*Companies reporting human health as a primary or secondary application.

**Includes scientific, technical, management, marketing, administrative personnel based in the U.S.

Table C.3b: Economic and Business Statistics, Averages by Company Size, Respondents Working in Agriculture and Aquaculture/Marine Applications, 2001

	Number of companies*	Employees ** Avg. (FTEs)	Net Sales Avg. ($ thousand)	Operating Income Avg. ($ thousand)	Capital Expenditures Avg. ($ thousand)	R&D Expenditures Avg. ($ thousand)
All companies reporting	128					
Entire business		1,640	$427,261	$76,508	$18,738	$25,289
Biotech activities		116	$28,341	–$730	$2,747	$9,877
Segment: > 15,000 employees	4					
Entire business		44,382	$13,446,667	$2,791,667	$539,100	$574,333
Biotech activities		1,200	$219,599	$22,880	$8,025	$72,886
Segment: 2,501–15,000 employees	2					
Entire business		5,315	$850,631	$58,931	$21,485	$12,619
Biotech activities		999	$300	–$1,478	$87	$1,656
Segment: 501–2,500 employees	8					
Entire business		1,378	$801,946	$78,622	$30,632	$59,472
Biotech activities		401	$157,323	$990	$9,007	$23,583
Segment: 51–500 employees	39					
Entire business		204	$82,069	$5,148	$8,109	$17,158
Biotech activities		103	$28,877	–$3,597	$5,527	$15,862
Segment: 11–50 employees	37					
Entire business		26	$2,320	–$1,537	$602	$2,134
Biotech activities		20	$1,945	–$1,501	$573	$2,123
Segment: 1–10 employees	37					
Entire business		5	$505	–$148	$62	$309
Biotech activities		4	$484	–$91	$60	$301

*Companies reporting animal health as a primary or secondary application.

**Includes scientific, technical, management, marketing, administrative personnel based in the U.S.

Table C.3c Economic and Business Statistics, Averages by Company Size, Respondents Working in Animal Health Applications, 2001

	Number of companies*	Employees ** Avg. (FTEs)	Net Sales Avg. ($ thousand)	Operating Income Avg. ($ thousand)	Capital Expenditures Avg. ($ thousand)	R&D Expenditures Avg. ($ thousand)
All companies reporting	144					
Entire business		1,271	$598,259	$109,621	$37,616	$50,666
Biotech activities		180	$124,025	$37,227	$18,287	$24,714
Segment: > 15,000 employees	4					
Entire business		40,871	$18,782,698	$3,506,620	$1,125,288	$1,440,152
Biotech activities		3,438	$3,576,104	$1,224,833	$506,313	$647,482
Segment: 2,501–15,000 employees	0					
Entire business		—	—	—	—	—
Biotech activities		—	—	—	—	—
Segment: 501–2,500 employees	9					
Entire business		1,166	$569,451	$92,281	$35,321	$61,932
Biotech activities		853	$195,928	$22,110	$15,503	$27,962
Segment: 51–500 employees	33					
Entire business		185	$64,505	$6,886	$5,359	$13,487
Biotech activities		99	$17,075	–$1,393	$3,550	$11,448
Segment: 11–50 employees	56					
Entire business		26	$2,547	–$971	$2,352	$2,207
Biotech activities		20	$2,172	–$1,027	$2,458	$2,242
Segment: 1–10 employees	41					
Entire business		5	$347	–$370	$63	$588
Biotech activities		4	$336	–$291	$62	$521

*Companies reporting animal health as a primary or secondary application.

**Includes scientific, technical, management, marketing, administrative personnel based in the U.S.

Table C.3d: Economic and Business Statistics, Averages by Company Size, Respondents Working in Industrial and Agriculture-derived Processing Applications, 2001

	Number of companies*	Employees ** Avg. (FTEs)	Net Sales Avg. ($ thousand)	Operating Income Avg. ($ thousand)	Capital Expenditures Avg. ($ thousand)	R&D Expenditures Avg. ($ thousand)
All companies reporting	132					
Entire business		3,302	$1,701,694	$329,965	$89,044	$110,808
Biotech activities		190	$52,504	$5,557	$4,829	$16,874
Segment: > 15,000 employees	9					
Entire business		40,443	$20,567,657	$3,742,208	$1,060,006	$822,001
Biotech activities		1,054	$448,637	$88,431	$12,703	$118,839
Segment: 2,501–15,000 employees	8					
Entire business		6,124	$6,361,752	$1,684,322	$316,803	$837,449
Biotech activities		820	$45,879	$17,867	$12,048	$57,310
Segment: 501–2,500 employees	9					
Entire business		1,399	$843,631	$70,200	$49,418	$52,539
Biotech activities		513	$153,865	$1,474	$10,468	$24,665
Segment: 51–500 employees	37					
Entire business		158	$190,972	$8,291	$9,376	$11,248
Biotech activities		97	$28,759	–$5,426	$5,123	$10,059
Segment: 11–50 employees	38					
Entire business		26	$3,741	$18	$3,375	$2,003
Biotech activities		19	$2,732	–$75	$3,314	$1,940
Segment: 1–10 employees	30					
Entire business		5	$528	–$244	$43	$355
Biotech activities		4	$466	–$261	$44	$368

*Companies reporting animal health as a primary or secondary application.

**Includes scientific, technical, management, marketing, administrative personnel based in the U.S.

Table C.3e: Economic and Business Statistics, Averages by Company Size, Respondents Working in Marine and Terrestrial Microbial Applications, 2001

	Number of companies*	Employees ** Avg. (FTEs)	Net Sales Avg. ($ thousand)	Operating Income Avg. ($ thousand)	Capital Expenditures Avg. ($ thousand)	R&D Expenditures Avg. ($ thousand)
All companies reporting	41					
Entire business		3,973	$1,268,769	$409,939	$89,473	$205,836
Biotech activities		209	$61,347	$7,700	$4,486	$14,900
Segment: > 15,000 employees	3					
Entire business		47,945	$24,726,000	$5,074,000	$1,494,000	$1,558,000
Biotech activities		333	$208,197	$14,760	$4,984	$106,285
Segment: 2,501–15,000 employees	2					
Entire business		6,315	$8,996,032	$4,320,380	$662,146	$2,477,863
Biotech activities		1,490	$599	$444	$14,614	$312
Segment: 501–2,500 employees	4					
Entire business		1,258	$373,883	$69,409	$18,790	$47,466
Biotech activities		937	$373,883	$69,409	$18,790	$47,466
Segment: 51–500 employees	6					
Entire business		165	$34,197	–$6,498	$8,709	$11,367
Biotech activities		84	$30,383	–$7,860	$5,409	$11,367
Segment: 11–50 employees	9					
Entire business		33	$2,005	–$2,635	$891	$2,440
Biotech activities		28	$2,005	–$2,635	$857	$2,440
Segment: 1–10 employees	17					
Entire business		5	$420	–$65	$52	$285
Biotech activities		5	$380	–$70	$50	$283

*Companies reporting animal health as a primary or secondary application.

**Includes scientific, technical, management, marketing, administrative personnel based in the U.S.

Table C.3f: Economic and Business Statistics, Averages by Company Size, Respondents Working in Environmental Remediation and Natural Resource Recovery Applications, 2001

	Number of companies*	Employees ** Avg. (FTEs)	Net Sales Avg. ($ thousand)	Operating Income Avg. ($ thousand)	Capital Expenditures Avg. ($ thousand)	R&D Expenditures Avg. ($ thousand)
All companies reporting	41					
Entire business		3,450	$1,760,286	$235,696	$148,561	$54,129
Biotech activities		149	$30,541	$2,876	$2,277	$11,532
Segment: > 15,000 employees	3					
Entire business		39,833	$16,910,667	$2,312,000	$1,521,667	$570,667
Biotech activities		1,569	$282,072	$33,164	$10,539	$92,807
Segment: 2,501–15,000 employees	2					
Entire business		9,230	$7,516,600	$1,134,000	$454,500	$38,970
Biotech activities		3	$0	–$50	$0	$157
Segment: 501–2,500 employees	2					
Entire business		1,228	$519,347	$11,698	$74,704	$45,500
Biotech activities		439	$112,437	$20,934	$16,729	$36,224
Segment: 51–500 employees	4					
Entire business		156	$17,345	–$7,607	$5,046	$15,567
Biotech activities		87	$11,214	–$10,050	$4,960	$14,669
Segment: 11–50 employees	7					
Entire business		22	$1,260	–$461	$117	$607
Biotech activities		13	$1,196	–$479	$115	$607
Segment: 1–10 employees	23					
Entire business		6	$513	–$93	$45	$119
Biotech activities		4	$422	–$105	$41	$114

*Companies reporting animal health as a primary or secondary application.

**Includes scientific, technical, management, marketing, administrative personnel based in the U.S.

Table C.3g: Economic and Business Statistics, Averages by Company Size, Respondents Working in "Other" Applications, 2001

	Number of companies*	Employees ** Avg. (FTEs)	Net Sales Avg. ($ thousand)	Operating Income Avg. ($ thousand)	Capital Expenditures Avg. ($ thousand)	R&D Expenditures Avg. ($ thousand)
All companies reporting	160					
Entire business		787	$491,341	$104,641	$30,924	$22,248
Biotech activities		93	$23,308	$526	$3,373	$7,682
Segment: > 15,000 employees	2					
Entire business		44,251	$30,107,150	$7,411,350	$1,623,693	$1,023,100
Biotech activities		120	$0	$0	$4,650	$66,812
Segment: 2,501-15,000 employees	4					
Entire business		4,715	$3,132,032	$207,234	$147,355	$129,089
Biotech activities		1,128	$411,032	–$3,291	$46,466	$109,215
Segment: 501–2,500 employees	10					
Entire business		839	$129,446	$19,231	$14,813	$29,255
Biotech activities		480	$77,893	$14,903	$8,517	$23,358
Segment: 51–500 employees	43					
Entire business		199	$37,491	$605	$13,986	$7,219
Biotech activities		99	$22,946	–$44	$4,054	$5,355
Segment: 11–50 employees	56					
Entire business		23	$2,519	–$790	$998	$1,441
Biotech activities		16	$2,361	–$690	$1,039	$1,160
Segment: 1–10 employees	44					
Entire business		6	$1,155	–$202	$345	$265
Biotech activities		4	$512	–$185	$27	$253

*Companies reporting animal health as a primary or secondary application.

**Includes scientific, technical, management, marketing, administrative personnel based in the U.S.

APPENDIX D
GLOSSARY[1]

[1] This appendix provides a brief list of technical terms used but not defined in either the survey or the main text of this report. Most of the terms relate to bioscience and technology. A few refer to the financial analysis of the biotechnology industry in this report. Additional sources for definitions and background information on science and technology include http://bio.org, http://www.ncbi.nlm.nih.gov/About/primer/index.html, and http://agnic.umd.ed/. For additional information on financial analysis terms and concepts see InvestorWords.com at http://www.investorwords.com, Universal Accounting at http://www. accounting-and-bookkeeping-tips.com/learning-accounting/, and Solution Matrix, Ltd.'s business case analysis Web site at http://www.solutionmatrix.com/.

A

Amino acids
Basic chemical building blocks of proteins. There are 20 common amino acids: alanine, arginine, aspargine, aspartic acid, cysteine, glutamic acid, glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine. In addition, two other amino acids have been discovered in microbes: selenocysteine and pyrolysine.

Antibody
A protein produced by humans and higher animals through an immune response to the presence of a specific antigen.

Antigen
A substance that, when introduced into the body, induces an immune response.

Antisense
One of an emerging set of "RNA interference" approaches in biotechnology, intended to modify a cell's normal processes of gene expression, for therapeutic purposes (e.g., to suppress the effect of genes involved in induction of human cancers) or to fine-tune the particular characteristics of commercially significant agricultural commodities (such as fruits with improved shelf life characteristics).

Aquaculture
Growth of aquatic organisms in controlled environment, particularly for marine food products. Application of biotechnology can help increase production, productivity, and quality, including improved genetic traits in fish and shellfish, growth factors, and defense mechanisms to fight microbial infections.

Assay (bioassay)
Analytical techniques to measure a biological response. For example, determination of the biochemical response of an animal cell system when exposed to a possible therapeutic compound.

B

Base pair
Two complementary nucleotide bases on opposite strands of the DNA molecule that weakly bond. Nature is strict in the pairings of bases allowed: adenine pairs only with thymine (DNA) or uracil (RNA), and guanine pairs only with cytosine.

Bioassay
Determination of the effectiveness of a compound by measuring its effect on animals, tissues, or organisms in comparison with a standard preparation.

Bioaugmentation
Increasing the activity of bacteria that break down pollutants by adding more of their kind. A technique used in bioremediation.

Biocatalyst
In bioprocessing, an enzyme that activates or speeds up a biochemical reaction.

Biodegradable
Capable of being reduced to water and carbon dioxide by the action of microorganisms.

Bioenrichment
A bioremediation strategy that involves adding nutrients or oxygen, thereby bolstering the activity of microbes as they break down pollutants.

Bioinformatics
The science of information as applied to biological research. Informatics is the management and analysis of data using advanced computing techniques. Bioinformatics is particularly important as an adjunct to genomics research, because of the large amount of data and complex relationships among bioactive molecules that this research generates.

Bioleaching
Use of natural or laboratory-altered microorganisms to extract and concentrate metals and other minerals from their location of deposit.

Biomass
The totality of biological matter in a given area. As commonly used in biotechnology, refers to the use of cellulose, a renewable resource, for the production of chemicals that can be used to generate energy or as alternative feedstocks for the chemical industry to reduce dependence on nonrenewable fossil fuels.

Biomaterials
Biological molecules (such as proteins, complex sugars) used to make devices such as structural elements for reconstructive surgery.

Biopharmaceuticals
Pharmaceutical drugs such as proteins, antibodies, and enzymes derived from biotechnology methods.

Bioprocess engineering
Process that uses complete living cells or their components (e.g., enzymes, chloroplasts) to effect desired physical or chemical changes.

Bioremediation
Use of natural or laboratory-altered microorganisms to degrade, detoxify, or accumulate contaminants for cleanup. Provides a control technology approach to render hazardous wastes nonhazardous.

Biosensors
Combination of molecular biology, advanced materials, and microelectronics to produce sophisticated monitoring devices capable of being activated by or measuring minute levels of bioactive molecules.

Biotransformation
The use of enzymes in chemical synthesis to produce chemical compounds of a desired stereochemistry.

C

Catalyst (biocatalyst)
An agent—such as an enzyme or a metal complex—that facilitates the kinetics of a chemical reaction.

Cell culture
Growth and maintenance of cells isolated from multicellular organisms in artificial (in vitro) conditions.

Chemical genomics
Use of structural and functional genomic information about biological molecules, especially proteins, to identify useful small molecules and alter their structure to improve their efficacy (e.g., as therapeutic drugs).

Clinical studies (clinical trials)
Generally, studies in human populations that are designed to measure the safety and efficacy of a new drug or other biologic treatment. Clinical trials come in various forms (Phases I, II, III) and are mandatory for new drugs and biologics under Food and Drug Administration (FDA) regulations. Complex experimental designs and control groups are typically involved in such trials.

Cloning
In recombinant DNA technology: the process of using a variety of DNA manipulation procedures to produce multiple copies of a single gene or segment of DNA.

Combinatorial chemistry
An approach to drug discovery that has evolved in recent years. The process enables rapid synthesis and screening of as many as several million molecules with similar structure in order to find molecules with desired properties. (See also *drug design*.)

Computational biology
A subdiscipline of bioinformatics, which involves chiefly computation-based research directed at understanding basic biological processes.

Confined release assessment (field trial)
Component of a government regulatory process in which an advance determination is made of the risk to the environment, including to health, of the release of an agricultural organism with novel features (e.g., seeds from a transgenic plant). Confined release is generally a research step, involving strict terms and conditions, such as reproductive isolation and restrictions in the use of the harvested material and field plot in subsequent growing seasons. (Compare with *unconfined release assessment*.)

Cost of goods sold (COGS)
The costs of producing goods and services sold. These may include production costs such as raw materials, supplies, and labor.

Cross-licensing
A legal, contractual procedure in which two or more firms with established intellectual property (IP) rights (e.g., a patent) to technologies mutually needed for continuing R&D and execution of company business plans strike a business deal (e.g., through mutual patent licensing) such that all parties can get access to the needed technologies. Cross-licensing helps to avoid both conflicts over IP rights and subsequent legal actions such as infringement suits.

D

Deoxyribonucleic acid (DNA)
Molecule that carries the genetic information for most organisms living on earth. The DNA molecule is comprised by a varied sequence of four nucleotide bases (adenine, cytosine, guanine, and thymine) along with a sugar-phosphate backbone. Structurally, these components are arrayed in paired strands that wind together in the form of a double helix.

Diagnostic tests
Laboratory and health care tools/products that can reliably measure biochemical and other biological parameters which are helpful in diagnosing disease or other medical conditions. Both monoclonal antibodies and DNA probes are useful diagnostic products.

DNA amplification
Process by which a very large number of copies of a target DNA sequence is synthesized (usually in a laboratory test tube). This kind of multiplication is normally needed for adequate DNA analysis in contemporary molecular biology. The widely known polymerase chain reaction (PCR) is frequently used to perform this amplification, which can quickly produce a million or more extremely accurate copies of a target sequence.

DNA hybridization
Procedure in which single-stranded nucleic acid segments are allowed to bind with complementary segments (following nature's nucleotide base pairing rules) to form a double-stranded helix.

DNA library
A large, systematic collection of DNA fragments. Such libraries help scientists to catalog and distinguish the millions, or even billions, of nucleotides in the genomes of organisms. There are many types of libraries. A "genomic library" contains all the different types of DNA sequences found in a genome (coding, noncoding, and repetitive DNA sequences). A "complementary DNA (cDNA) library" includes only genes that are expressed, i.e., genes that get transcribed in messenger-RNA, which is then translated into proteins. A "chromosome-specific library" focuses on the DNA associated with a single chromosome.

DNA microarray (Gene chip, Genome chip)
A recent new technology in the field of molecular biology and genetics. The microarray is a laboratory microscale sampling and analysis membrane which systematically incorporates many different DNA probes. An experiment with a single DNA microarray can provide research information on the involvement of thousands of genes in cellular functions.

DNA polymerase
An enzyme that replicates DNA. DNA polymerase is the basis of the polymerase chain reaction.

DNA probes
Various analytical techniques have been developed, based on the hybridization process and its selective base pairing logic, to locate a specific sequence along a DNA strand. A short piece of DNA (a "probe"), which is complementary to a nucleotide sequence of interest (and often explicitly synthesized for this purpose), is mixed with the target DNA strand. As a result of hybridization, the probe will bind and form a region of double-stranded DNA wherever the probe sequence encounters a complementary sequence along the target DNA strand. Such areas of hybridization are typically identified and analyzed through standard laboratory blotting and radiographic methods.

DNA sequencing
Identification of the specific sequence of nucleotide bases (adenine, cytosine, guanine, thymine) that comprise a segment of DNA. Cutting-edge laboratory technology and computers have greatly automated the chemical and analytical steps needed for these determinations. The recently completed international project to sequence the human genome involved identifying some 3 billion nucleotide base pairs.

DNA synthesis (oligonucleotides)
Current biotechnology methods enable a wide range of artificial DNAs, with known base sequences in one or more regions, to be synthesized for use as tools and reagents for laboratory research and diagnostic test applications. In fact, the principal purpose of a significant segment of the present biotechnology industry is preparing such oligonucleotides to commercial order, at high accuracy and purity.

Drug delivery
Process by which a formulated drug is administered to a patient. The traditional routes have been oral or intravenous perfusion. New methods provide for delivery through the skin with a transdermal patch or across the nasal membrane with an aerosol spray.

Drug design (rational drug design)
The now rapidly advancing scientific knowledge of cell functions in molecular terms, in both healthy and disease states, and improved ability to model the chemical and biological pathways involved provide an improved basis to infer the chemical identity and three-dimensional structure of molecules with likelihood of providing positive therapeutic effects. This "rational approach" to drug design stands in some contrast to the long-standing prior approach in which the identification of new therapeutic drugs depended chiefly on dose-response screening (often serendipitous) of many molecules for biological activity.

E

Enzyme
A protein catalyst that promotes specific chemical or metabolic reactions necessary for cell functioning and development.

Expression
In genetics, manifestation of a characteristic that is specified by a gene. With hereditary disease, for example, a person can carry the gene for the disease but not actually have the disease. In this case, the gene is present but not expressed. In industrial biotechnology the term is often used to mean the production of a protein by a gene that has been inserted into a new host organism.

Extraction, separation, purification
Process of isolating a compound of interest in a mixture of many compounds and refining the purity. Is a standard problem in most all chemistry, irrespective of the state of matter (solid, liquid, gas) at hand. In biotechnology, this problem often arises as a need to identify, isolate, concentrate, and/or purify specific proteins, gene fragments, or other bioactive molecules from the integrated, functioning cells in which they naturally exist.

Extremophiles
Microorganisms that live at extreme levels of pH, temperature, pressure, and salinity. An example is the Taq polymerase, which facilities the widely used polymerase chain reaction (PCR) technique for quickly amplifying nucleotide chains. This enzyme was isolated from the thermophilic bacterium *Thermus Aquaticus,* which exists in hot spring-like conditions.

F

Fermentation
An (anaerobic) process for growing microorganisms for the production of various chemical or pharmaceutical compounds. Microbes are normally incubated under specific conditions in the presence of nutrients in large tanks called fermentors.

Functional foods (nutraceuticals)
Foods containing compounds with beneficial health effects beyond those provided by the basic nutrients, minerals, and vitamins.

Functional genomics
A field of research that aims to understand what each gene does, how it is regulated and how it interacts with other genes. (See also *genomics*.)

G

Gene
The fundamental physical and functional unit of heredity. A segment of a chromosome. An ordered sequence of nucleotide base pairs that produce a specific product or have an assigned function. Some genes direct the syntheses of proteins, while others have regulatory functions.

Gene mapping
Determination of the relative locations of genes on a chromosome. Genetic maps use landmarks called genetic markers—any observable variation that results from a known **alteration** or mutation at a specific genetic locus—to guide scientists in the hunt for the specific physical location of a gene on a chromosome.

Gene therapy
Replacement of a defective gene in an organism suffering from a genetic disease. Recombinant DNA techniques are becoming increasingly more able to successfully insert a functional form of the gene into relevant cells, thereby relieving the disease. More than 300 single-gene genetic disorders have been identified to date in humans. A significant percentage of these may be amenable to gene therapy.

Genetic engineering (Genetic modification)
Various techniques now available—such as selective breeding, mutagenesis, transposon insertions, and recombinant DNA technology—that can be used to alter the genetic material of cells in order to make them capable of producing new substances, performing new functions, or blocking the production of substances.

Genetic screening
Use of genetic analysis procedures to screen for inherited diseases or medical conditions. Testing can be conducted prenatally to check for metabolic defects and congenital disorders in the developing fetus, as well as postnatally to screen for carriers of heritable diseases.

Genetics
The scientific study of heredity and how particular qualities or traits are transmitted from parents to offspring.

Genome
All the genetic material in the chromosomes of a particular organism. Its size is generally measured as its total number of nucleotide base pairs.

Genomics
The scientific study of genes and their functions. Recent advances in genomics are bringing about a revolution in our understanding of the molecular mechanisms of disease, including the complex interplay of genetic and environmental factors. Genomics is also stimulating the discovery of breakthrough health care products by revealing thousands of new biological targets for the development of drugs and by giving scientists innovative ways to design new drugs, vaccines, and DNA diagnostics. Genomic-based therapeutics may include "traditional" small chemical drugs, protein drugs, and gene therapy.

Genotype
The genetic constitution of an organism. (Compare with *phenotype*.)

H

Hormone
A protein or other biochemical that acts as a messenger or stimulatory signal, relaying instructions to stop or start certain physiological activities. Hormones are synthesized in one type of cell and then released to direct the function of other cell types.

I

Immunodiagnostics
The use of specific antibodies to measure a substance of interest. This kind of analytical tool is useful in diagnosing infectious diseases and the presence of foreign substances in a variety of human and animal fluids.

Immunology
The study of the biology and biochemistry of the body's immune response to pathogens and other foreign substances.

Inducer
A molecule or substance that increases the rate of enzyme synthesis, usually by blocking the action of the corresponding repressor.

M

Microbial ecology
General reference to the biological nature and interrelationships of the system of microorganisms in an ecosystem.

Microbial herbicides and pesticides
Microorganisms that are selectively toxic to specific plants or insects. Because of their narrow host range and limited toxicity, these microorganisms can be preferable to conventional synthetic chemical herbicides and pesticides for certain pest control applications.

Molecular genetics
Study of how genes function to control cellular activities.

Monoclonal antibody (MAb)
A highly specific, purified antibody derived from a single clone of specialized cells that recognizes only one antigen.

N

Net revenues
Total of all receipts of an enterprise. This may include receipts from sales of products, services, or merchandise; and earnings from interest, dividends, rents, wages, and technology licensing.

Net sales
Gross receipts from sales of goods or services minus returns, discounts, or allowances.

Nucleotide (nucleotide base)
The building blocks of nucleic acids such as DNA and RNA. Each nucleotide is composed of sugar, phosphate, and one of four nitrogen bases. The sugar in DNA is deoxyribose and RNA's sugar is ribose. The sequence of the bases along the nucleic acid's molecular chain directs the synthesis of the sequence of amino acids in a protein.

O

Operating income
A measure of a company's earning power from ongoing operations. In the present survey, operating income is defined as net sales minus the cost of goods sold and selling, general, and administrative expenses.

P

Pharmacogenetics
Study of hereditary influences on drug response.

Phenotype
Observable characteristics of an organism produced by the organism's genotype interacting with the environment. (Compare with *genotype*.)

Phytoremediation
The use of plants to clean up pollution.

Pre-clinical studies
Studies that test a potential new drug, diagnostic, or other medical treatment on animals and in other nonhuman test systems. For example, safety information derived from such studies is often used to support an Investigational New Drug application (IND) filed with the Food and Drug Administration (FDA).

Protein (polypeptide)
A molecule composed of a chemically linked sequence of amino acids. There are many types of proteins, and each cell produces thousands of proteins. These proteins carry out different functions essential for cell functioning and development.

Protein sequencing
The process of ascertaining the identity and order of the amino acids that comprise a protein molecule of interest.

Proteomics
The set of proteins in a cell is termed the proteome. Unlike the genome, which is constant irrespective of cell type, the proteome varies from one type of cell to another. The science of proteomics strives to characterize the protein profile of each cell type, assess protein differences between healthy and diseased cells, and analyze each protein's specific function and how it interacts with the other proteins in the cell.

R

Radioimmunoassay (RIA)
A test combining radioisotopes and immunology to detect trace substances. Such tests are useful for studying antibody interaction with cell receptors and can be developed into clinical diagnostics.

Recombinant DNA
General reference to the broad range of techniques involved in manipulating genetic material in organisms. The term is often used synonymously with "genetic engineering."

Recombination
The process of breaking and rejoining DNA strands, which occurs naturally in the course of cellular functioning. This produces new combinations of genes and, thus, generates genetic variation.

Research tools
In the realm of contemporary biotechnology R&D, this term is frequently used to refer to genes, gene fragments, DNA mutations, and related proteins, whose biochemical identity and availability as isolated molecules are regarded as essential foundations for productive further research in molecular biology.

Restriction fragment length polymorphism (RFLP)
The variation in the length of DNA fragments produced by a restriction endonuclease that cuts at a polymorphic locus. This is a key tool in DNA fingerprinting and is based on the presence of different alleles in an individual. RFLP mapping is also used in plant breeding to see if a key trait such as disease resistance is inherited.

Ribonucleic acid (RNA)
Also a nucleic acid, composed of a chemically linked sequence of nucleotide bases. RNA exists in three forms (messenger RNA, transfer RNA, and ribosomal RNA) responsible for translating the genetic information encoded in an organism's DNA into the proteins essential for cell functioning and development. RNA is also the hereditary material for some viruses.

RNA interference
An emerging approach to genetic engineering—whether in developing new therapeutic drugs or organisms with altered traits—that seeks to selectively influence the cellular processes of RNA translation and transcription that yield the proteins essential for cellular functioning.

S

Selling, general, and administrative expenses (SGAE)
Expenses and costs not linked to the production of specific goods, but including all selling, general company expense, and administrative expenses. These expenses may include salespersons' salaries, advertising, salaries for executives, and other administrative expenses.

Somatic cell gene therapy
Gene therapy approach that involves inserting genes into cells for therapeutic purposes—for example, to induce such treated cells to produce a protein that the body is missing. This does not affect the genetic makeup of a patient's offspring and generally does not change all, or even most, cells in the recipient. Somatic cell gene therapy is one of several possible ways use genomics to improve health care.

Structural biology
Biological science that focuses on systematic understanding of the biological structures that both distinguish different organisms and allow them to function.

Structural gene
A gene that codes for a protein, such as an enzyme.

Systems biology
A hypothesis-driven field of research that creates predictive mathematical models of complex biological processes or organ systems.

T

Three-dimensional molecular modeling
Typically, this is directed at identifying a protein's shape (structure). The three-dimensional structure of these molecules—beyond simple chemical composition and amino acid sequence—is increasingly recognized as key in determining biological function. Identifying this structure is, however, no easy analytical feat. Present methods involve such tools as X-ray crystallography, nuclear magnetic resonance spectroscopy, and extensive computer modeling.

Transcription, Translation
Critical cellular processes, involving DNA and RNA, involved in transforming genetic information in synthesized proteins essential for cell functioning and development. Transcription is synthesis of messenger RNA (mRNA) from the genetic (DNA) template. Translation is the process of turning the mRNA instructions (nucleotide sequence) into polypeptide chains of amino acids, which then fold into proteins.

Transgenic organism
Animals, plants, microbes, and other organisms whose hereditary DNA has been augmented by the addition of DNA from a source other than parental germplasm. Such organisms are made possible by the availability of recombinant DNA techniques.

U

Unconfined release assessment
Component of a government regulatory process whereby an advance determination is made of the risk to the environment, including to health, of the release of an agricultural organism with novel features (e.g., seeds from a transgenic plant). Unconfined release generally means release into the environment with limited or no restrictions (i.e., near to release associated with full product commercialization). (Compare with *confined release assessment*.)

V

Vaccine
A preparation of attenuated or killed microorganisms (e.g., viruses or bacteria) that when inoculated is capable of conferring immunity or otherwise counteracting the pathological effects of the original microorganisms. Until recently, vaccines have been prepared through natural or synthetic processes. However, the recombinant DNA techniques now provide a way to modify the genetic content of these microorganisms in ways that yield much more effective vaccines with fewer side effects.

Value added
An industry's net addition to gross domestic product. The term "net" signifies that purchases from other industries have been subtracted out of the gross sales of the industry to eliminate double-counting.

Virology
The scientific study of viruses and viral diseases.

Virus
Any of a large group of organisms containing genetic material, but which are unable to reproduce outside a host cell. To replicate, a virus must invade another cell and use parts of that cell's reproductive machinery

X

Xenobiotics
Synthetic chemicals believed to be resistant to environmental degradation. A branch of biotechnology called bioremediation is seeking to develop biological methods to degrade such compounds.