

# Biotechnology Sector Report

## Technology Roadmap Project



For the

**CENTER FOR ECONOMIC GROWTH**

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Prepared by:



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# BIOTECHNOLOGY / LIFE SCIENCES

## 1. Defining the biotechnology industry

### 1.1 Definition of biotechnology industry by technology:

Biotechnology, as a term used to define a set of technologies, usually refers to the application of molecular and cellular processes to solve problems, conduct research, and create goods and services. Under this technology based definition, biotechnology includes a diverse collection of technologies that manipulate cellular, subcellular, or molecular components in living things for applications in various scientific fields and industries such as medicine, animal health, agriculture, marine life, and environmental management <sup>1</sup>. A relevant term also used for core biotechnology-based companies is **life sciences or biosciences companies** and these terms will be used interchangeably with **biotechnology** in this report. Companies in the biotechnology industry are most frequently classified into the two following industrial NAICS codes:

NAICS 5417 – Scientific Research and Development Services

NAICS 541710 (SIC 8731) R&D in the Physical Engineering and Life Sciences;

and

NAICS 3254 Pharmaceutical and Medicine Manufacturing

NAICS 325411-325414 Medicinal, Botanical, Pharmaceutical preparation, in vitro  
(SIC 2833-2836) diagnostic substance and biological product manufacturing

### 1.2 Definition of biotechnology industry by application <sup>2</sup>:

Biotechnology as a technology has an impact on several industries broadly classified as:

Human and animal therapeutics and diagnostics – including biopharmaceutical companies  
Also includes tool developers - genomics, bioinformatics, proteomics companies and  
companies developing advanced materials for human therapeutics

*NAICS 3254 Pharmaceutical and Medicine Manufacturing*

*NAICS 5417 Research and Development in the Physical, Engineering, and Life Sciences*

Agriculture, aquaculture, animal health and food – includes seed and livestock development.

*NAICS 3253 Pesticide, Fertilizer, and Other Agricultural Chemical Manufacturing*

*NAICS 32519 Other Basic Organic Chemical Manufacturing*

*NAICS 11511, 11521 Support Activities for Crop and Animal Production*

*NAICS 112 Animal Production; raise animals for the sale of animals or animal products*

*NAICS 5417 Research and Development in the Physical, Engineering, and Life Sciences*

Industrial and agriculture derived processing – including chemical manufacturing companies

*NAICS 32519 Other Basic Organic Chemical Manufacturing*

*NAICS 32531, 32532 Pesticide, Fertilizer, and Other Agricultural Chemical Manufacturing*

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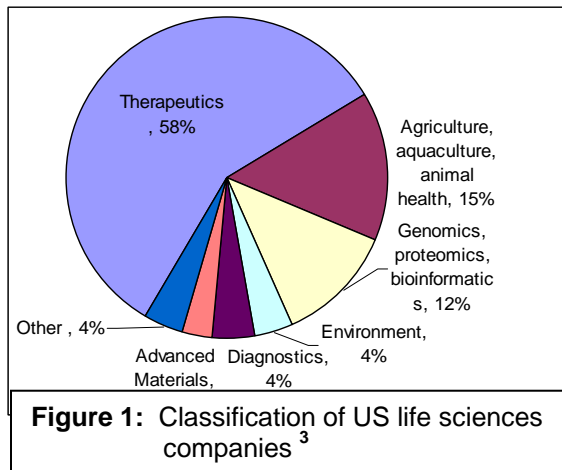
<sup>1</sup> *A survey of the use of biotechnology in U.S. industry*, US Dept of Commerce publication, October 2003.

<sup>2</sup> European Classification of Biotechnology: EuropaBio has given biotechnology applications a color to help differentiate between them. White biotech mostly refers to the industrial manufacturing of products using microorganisms and enzymes to make goods like vitamins, detergents, biofuels, etc. Green biotechnology refers to biotechnology used in agricultural applications and red biotechnology deals with biotechnologies applied to human medicine, diagnostics and new therapies.

Environmental remediation – including utilities, petroleum industry.  
NAICS 5629 Waste management and remediation services

However, the majority of biotechnology companies (58%<sup>3</sup> to 74%<sup>4</sup>) are focused on health care applications, with 98% of all economic activity in this sector reported by these life sciences companies<sup>4</sup>. Since these companies incorporate the critical leading advances in genomics, proteomics and related technologies and science, they also serve as leading indicators of the

growth in other applications of the life sciences and are used as the primary group for analysis of this technology / industry.



Within the above broad classifications, there are many sub-sectors defined by a complex mix of technology class and application space.

However, it is equally necessary to define what biotechnology is not. Biotechnology does not include medical technology (devices and instruments), high-tech medicine or medical informatics for medical records, as these disciplines are unconnected to genetic and cellular manipulation. An important exception to

this group is the production of software and tools for gene sequencing and analysis (bioinformatics).

*An extension of the pharmaceutical industry?* Among health applications, biotechnology companies are primarily defined as those with services and products based on life sciences, not traditional chemically synthesized products, as typical in the pharmaceutical (pharma) industry until a few decades ago. However, these distinctions are blurring as mature biotechnology companies are slowly becoming indistinguishable from large pharmaceutical companies.

## 2. Industry status, markets and outlook:

### 2.1 Current Status in USA

There are about 1,466 life sciences firms in the U.S., employing a total of 194,600 persons. Between 1993 and 1999, the industry doubled in size. The life sciences industry is dominated by small firms: the median biotechnology firm has 31 employees, annual revenues of \$4.5 million, and is highly dependent on innovation for continued financing.

There are more than 370 biotech drug products and vaccines currently in clinical trials targeting more than 200 diseases, including various cancers, Alzheimer's disease, heart disease, diabetes, multiple sclerosis, AIDS and arthritis<sup>5</sup>. This is an R&D intensive industry, which spends an

<sup>3</sup> *Resilience: Americas Biotechnology Report*, Ernst and Young, 2003

<sup>4</sup> *A survey of the use of biotechnology in U.S. industry*, U.S. Department of Commerce Technology Administration and Bureau of Industry and Security publication, October 2003.

<sup>5</sup> Biotechnology Industry Organization [www.bio.org](http://www.bio.org)

average of \$121,000 per employee on R&D (compared to pharma's \$30,600), and employees workers with an average wage about 85% higher than the average for all other sectors.

## 2.2 Global revenues distribution

Globally, the industry generated revenues of about \$43 billion in 2002, with the bulk of those revenues (\$30 billion) captured by US companies (Figure 2, 3)<sup>6</sup>. These revenues have shown a 20% growth rate over the last few years and are projected to continue at this rate for the next four years, exceeding \$125 billion by 2008. Correspondingly, the total number of life sciences companies in the US continues to grow (Figure 4, 5) with active mergers and partnering.

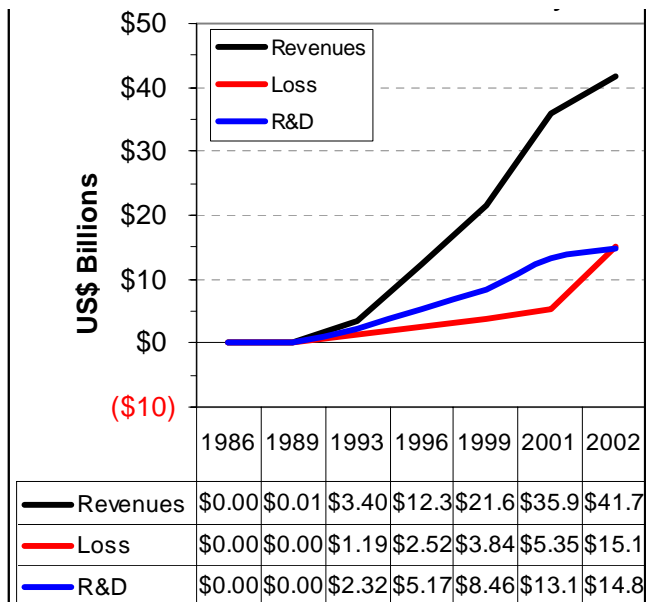


Figure 2. Global financials<sup>7</sup>

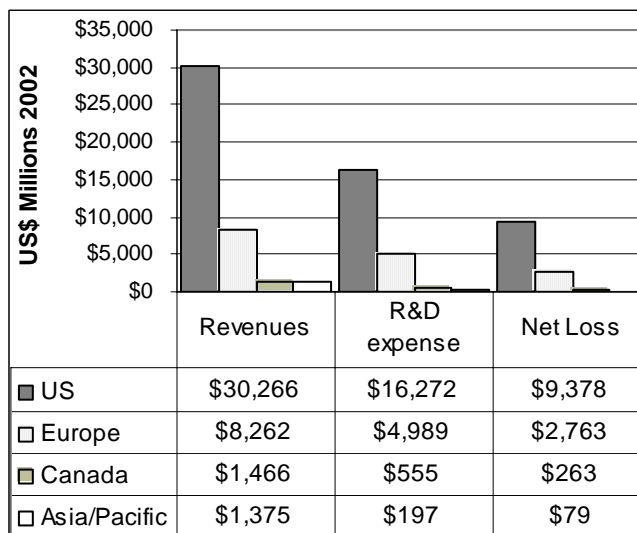


Figure 3. Global distribution of revenues

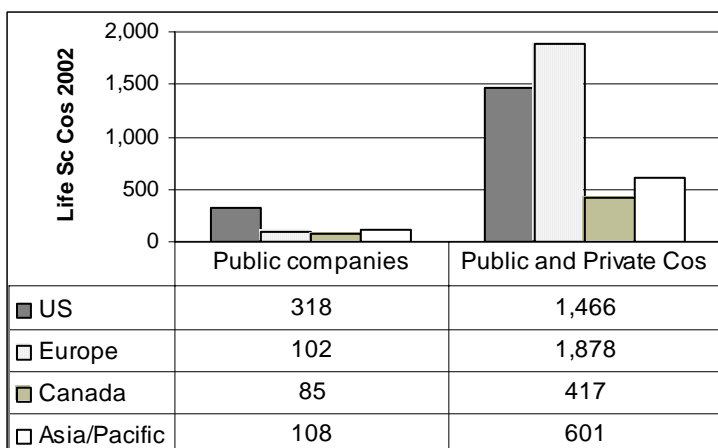


Figure 4: Global distribution of life sciences companies

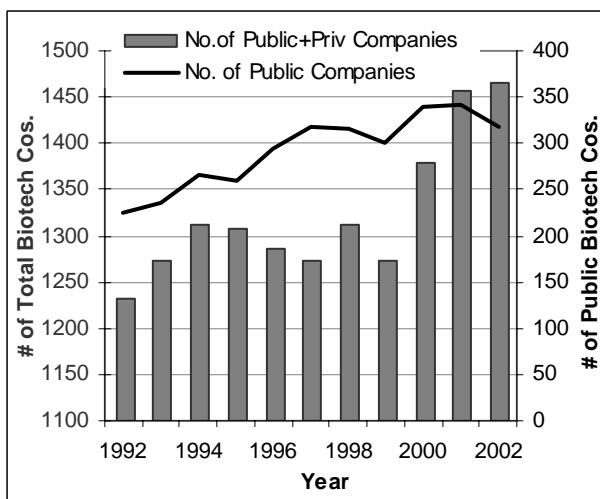
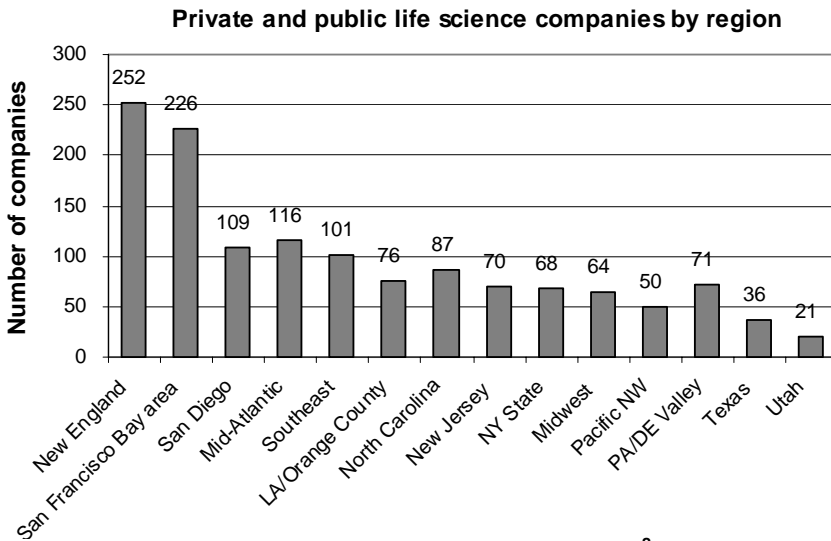


Figure 5: US life sciences companies growth

<sup>6</sup> Beyond borders: The global biotechnology report, Ernst and Young, 2003.

<sup>7</sup> Source: Nature Biotechnology – presentation by editor

### 2.3 USA regional distribution of life sciences companies

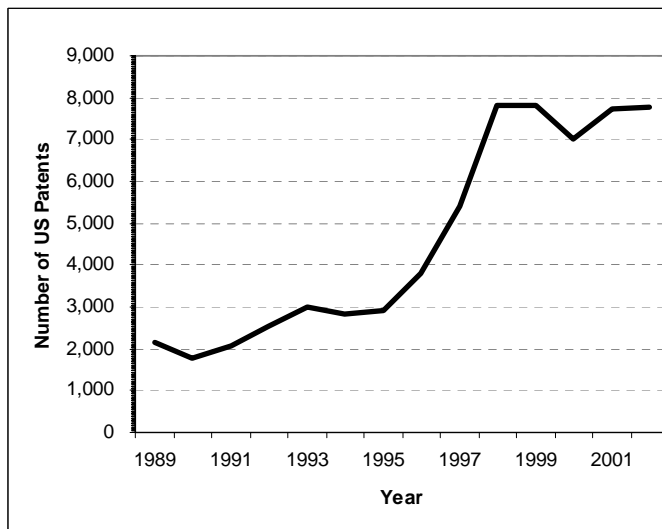


These US companies are primarily located in nine metro areas. These nine areas account for three-fourths of the nation's largest biotechnology firms and for three-fourths of the biotech firms formed in the past decade.

Cortright, J and Mayer, H, *Signs of Life*, The Brookings Institution Center on Urban and Metropolitan Policy, 2002.

Figure 6: Life Science Companies – clusters in the US <sup>8</sup>

### 3. Technology trends



Patent data underscore the dynamic and rapidly evolving nature of biotechnology. Patents are vital to the development of this industry. In the last quarter of 2002, respondents to the Department of Commerce survey of biotechnology companies indicated that they had pending U.S. patent applications for 33,131 new biotech-related products or processes, compared to 23,992 current U.S. biotechnology-related patents in their portfolios <sup>9</sup>.

Figure 7 Biotechnology patents in USA  
Sources: US Patent and Trademark Office and BIO

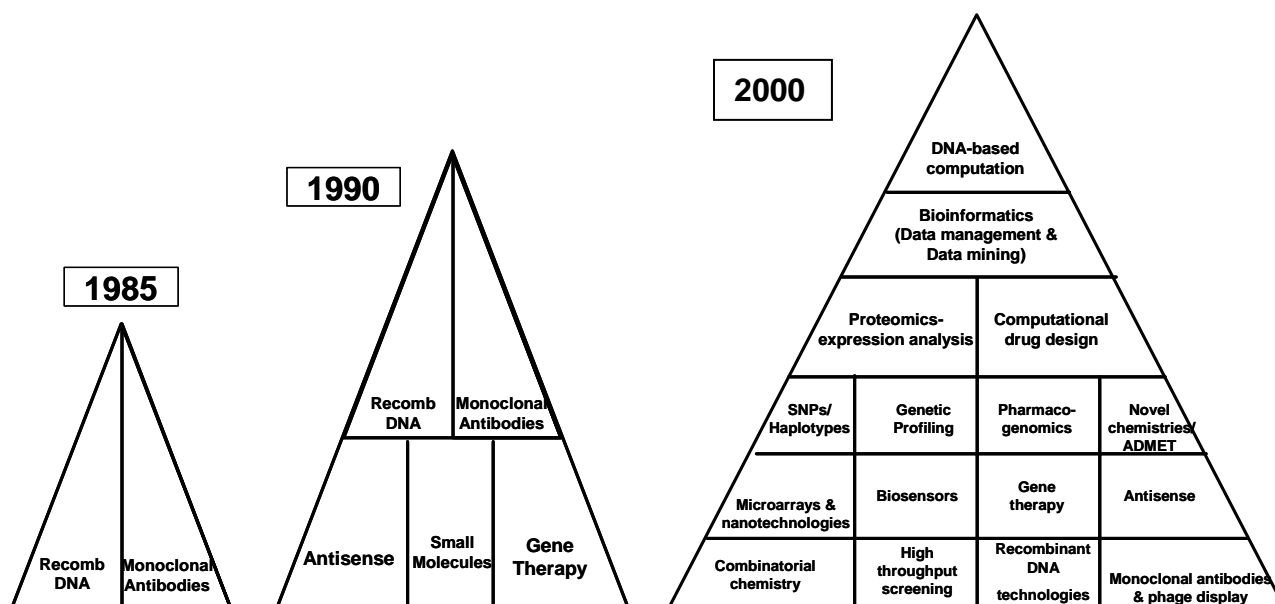
#### 3.1 Key technology milestones:

The modern concepts of life sciences could reasonably be said to have started with the elucidation of the structure of the DNA molecule by Watson and Crick in 1953. The application of biotechnology in the pharmaceutical industry started in the mid-1970s, with the development of key scientific techniques, mainly genetic engineering and antibody production.

<sup>8</sup> *Global Biotechnology Industry Report: Beyond Borders*, Ernst & Young LLP, 2003 and [www.bio.org](http://www.bio.org).

<sup>9</sup> *A survey of the use of biotechnology in U.S. industry*, U.S. Department of Commerce Technology Administration and Bureau of Industry and Security publication, October 2003.

However, an industry that started off with these two basic technologies in 1985, recombinant DNA (rDNA) and monoclonal AntiBody (mAB) production, has now accumulated several breakthroughs in its technology platforms, leading to an ever-increasing range of applications going beyond basic manufacturing techniques to enhance the entire supply chain in drug and diagnostic development as shown in Figure 8<sup>10</sup>.



**Figure 8:** Technology evolution and growth in the life sciences.<sup>9</sup>

### 3.2 Emerging and existing technologies in the life sciences industry

#### DNA-based:

HapMap (Haplotype Map) Project (completion date 2005), diagnostic gene testing; gene probes, DNA markers, DNA chips, Bioinformatics, Genomics, pharmacogenetics, DNA sequencing/synthesis/, amplification, genetic engineering, gene therapies and vaccines.

#### Biochemistry/Immunology:

Vaccines/immune stimulants, drug design & delivery, diagnostic tests, antibiotics, synthesis/sequencing of proteins and peptides, cell receptors/signaling, structural biology, combinatorial chemistry, 3-d molecular modeling, biomaterials, microbiology, virology, microbial ecology, proteomics; metabolomics.

#### Bioprocessing-based:

Culturing/manipulation of cells, tissues, embryos, stem cells, gene therapy, extractions, purifications, separations, Fermentation, bioprocessing, biotransformation.

#### Environmental:

Bioleaching, biopulping, biobleaching, biodesulfurization, bioremediation, biofiltration

### 3.3 Overlap with other emerging technology areas

Recent discovery, development, and application of life sciences are not only creating entirely new types of products and services, but biotech processes and products are now applied in all types of manufacturing, agriculture, aquaculture, and even at the microbial and nano-scales. Biotechnology has convergent applications with other technologies such as IT, Nanotech, Advanced Materials and Energy as reflected in Figure 8.

<sup>10</sup> Figures adapted from Alta Partners data presentation.

## 4. Industry drivers

The surge in public companies in the year 2000 in the USA resulted from the confluence of a number of coincident singular events – a large number of biological product approvals (32), lively public financing markets with high valuations and appetite for new technologies and the completion of the Human Genome Project<sup>11</sup>. Although the number of product approvals per year has since dropped to 24, it is expected to stabilize to about 21 per year over the next few years<sup>12</sup>. The Human Genome project brought the life sciences industry to the public view and the interest in this industry continues unabated, largely due to its potential to significantly impact our daily lives and health.

### 4.1 Demographics

An aging population worldwide will spend more on health care over the next few decades, driving growth in the health care industry, in which life sciences plays a key role. The global population over 65 years of age is forecast to rise from 380 million in 1997 to nearly 700 million by 2025. In the US alone, people 65+ represented 12.4% of the population in the year 2000 but are expected to grow to be 20% of the population by 2030. The elderly are the single largest group of users of prescription drugs, consuming three times as many pharmaceutical medicines as younger patients do. These demographics ensure an expanding global market for cutting-edge biotech, pharmaceuticals, and medical devices.

### 4.2 Financing

The life sciences industry is still in net loss and its long and expensive development cycles need external capital. The presence of private and public investments has been mentioned as a driver. There continues to be an influx of capital into the industry from government, venture capital, public markets and pharmaceutical partnerships.

**NIH:** Total NIH spending for research has more than doubled during the 1990s, from about \$6.5 billion in 1991 to more than \$13 billion in 2000. Congress approved a total fiscal-year 2003 budget of more than \$27.3 billion for NIH, an increase of 16% over the previous fiscal year; however, the 2004 budget has only a 1% increase over the previous year<sup>13</sup>.

**Venture capital:** The biotechnology industry raised \$2.1 billion in all venture capital financing in 2002, and almost \$2.5 billion in 2003, which is greater than twice the 1997 levels of \$1 billion<sup>14</sup>. Proximity to venture capital is a key factor in the formation and growth of life science clusters.

**Pharmaceutical R&D Investment, Outsourcing and M&A:** The pharmaceutical industry acts as the commercialization arm for life sciences companies and plays a significant role in financing. Global pharmaceutical R&D is projected to grow to about \$70 billion in 2007 from \$41.8 billion spent in 2000<sup>15</sup>. The R&D outsourcing market is predicted to grow from \$9.3 billion in 2001 to \$36.0 billion by 2010, representing an average annual growth rate of 16.3%.

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<sup>11</sup> [http://www.ornl.gov/sci/techresources/Human\\_Genome/home.shtml](http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml) Last accessed 15 March 2004.

<sup>12</sup> Acumen Journal, Vol II, Number II, p.45. March 2004

<sup>13</sup> [www.nih.gov](http://www.nih.gov) National Institutes of Health website.

<sup>14</sup> *Resilience: Americas Biotechnology Report* Ernst and Young, 2003.

<sup>15</sup> *Parexel's Pharmaceutical R&D Statistical Sourcebook*, Parexel Inc., 2003.

Contract research organizations will focus increasingly on higher profitability services such as preclinical and bioanalytical testing, laboratory services, drug discovery and informatics <sup>16</sup>.

#### **4.3 New discoveries, products and technologies**

All life science industry clusters are located in proximity to a major research university with high levels of NIH funding <sup>17</sup>. Increasing levels of biotechnology patents are driving the industry growth, as many small firms develop and sell these patents to large pharma or other partners to finance their internal R&D and continue innovating. New technologies that are being developed through aggressive R&D investments and the introduction of new products is a primary driver for growth in the industry.

#### **4.4 Regulatory changes**

Regulatory uncertainty remains very high, with only 70% - 75% of submitted applications making it past the final review process. However, recent changes are positive for the industry. The FDA approval cycles have been shortening (from over 20 months to 12 months in 1999 before going up to a 15 month approval cycle in 2000) with increased efficiency and better guidance being issued. The percentage of NMEs (new molecular entities) that are approved within 12 months of submission has remained relatively constant in recent years at around 40% <sup>18</sup>. The FDA has committed to working closely with sponsors to help prevent repeat submissions.

## **5. SUMMARY**

### **5.1 Relevance to economic development**

As healthcare expenditure already equals about 14% of the national GDP and continues to grow, there is little doubt that the life sciences industry will play a major role in the economy of the country and of the globe. Some estimates put the life sciences occupying about 12-14% of the GDP over the next two decades, making it a multi-trillion dollar industry.

This relatively new industry already has a significant impact on regional and national economies. In 1999, the combined direct, indirect and induced activities of the life sciences industry contributed a total of 437,400 jobs and \$47 billion in business revenues to the U.S. economy. The public sector also benefited significantly from the life sciences industry through additional federal, state and local taxes, estimated to be \$10 billion in 1999 <sup>19</sup>.

Direct impact - \$20.2 billion in 2001 from revenues, with 150,800 employees supported.

Indirect impact through purchases of equipment, materials, services etc = \$4.8 Billion in revenues to non life sciences companies, with 45,000 employees supported in these companies

Induced impact: purchases, exchange of goods and services = revenues of \$21.5 Billion into the consumer goods and services industry, with 241,600 employees supported in this industry.

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<sup>16</sup> *Pharmaceutical R&D outsourcing strategies*, Reuters Business Insight Healthcare report: 2002.

<sup>17</sup> Cortright, J. and Mayer, H., *Signs of Life*, The Brookings Institution Center on Urban and Metropolitan Policy, 2002.

<sup>18</sup> US Food and Drug Administration [www.fda.gov](http://www.fda.gov)

<sup>19</sup> "Economic Contributions of the Biotech Industry to the U.S. Economy," report prepared by Ernst & Young for the Biotechnology Industry Organization (BIO), May 2000 (accessed at [www.bio.org](http://www.bio.org)).

It has been estimated that for every direct job created by life sciences, roughly two additional indirect jobs are created in support services such as business supplies and legal services and in related consumer spending <sup>20</sup>.

According to the Brookings Institute report on life sciences cluster formation:

**The formation and flourishing of biotechnology firms ought ultimately to be the objectives of biotechnology development strategies and the result of an effective combination of research capability, knowledge creation activity, and investment capital.**

## 5.2 Sub sector attractiveness and growth listed in decreasing order of attractiveness

Sub-sector	Technology/ Product	Growth	Issues, Drivers
<b>Biopharmaceutical companies</b>	Primarily human monoclonal antibodies and biological drugs, vaccines.	16-20% CAGR growth over the next four years. US public companies revenues increasing to about \$60 billion by 2007.  (E&Y, industry reports, BCC research reports, BIO)	Expected new biologic products approvals (accounting for failures in current pipeline of over 370 products) in the next four to six years.
<b>In vitro diagnostics and biosensors</b> (includes clinical diagnostics) <b>Research Tools</b> such as – Drug target screening, ID and validation	Nucleic tests, Microarrays, laboratory testing, point-of-care testing, Bioinformatics, Pharmacogenomics, Proteomics	Worldwide (WW) 2003 \$ 23 billion 15-20% growth over next four years (NES reports) 2007 \$48 billion 2010 \$83 billion  (Sources: Kalorama Information Research and BCC research reported in Acumen vol II(II): 60, Mar 2004; NES reports.)	Acceptance of surrogate markers in clinical trials, increasing use of tools to assess drug failure or success before in vivo testing. High throughput technologies and automation, partnership between therapeutics and diagnostics. Overlap with materials and nanotech sectors.
<b>Industrial Biotech (White biotech)</b>	Bioprocessing; biomanufacturing novel enzymes.	By 2010 industrial biotech will generate about \$470 billion WW with a \$160 billion value impact on chemicals. (Burrill and Co. Dec'03)	Industrial biotechnology applications are increasing within established industries – food processing, energy, chemicals, environmental remediation.
<b>Gene and cell therapy (regenerative medicine)</b>	Cell replacement, gene delivery, siRNA, stem cell research, cancer therapies.	Cell therapy market WW is about \$20.2 billion in 2002, \$35.7 billion projected by 2007. (Jain Pharmabiotech reports).  The global market for regenerative medicine could be worth in excess of \$30 billion in 10 years (Cambridge Consultants report).	The emphasis will continue to be on cancer therapy as the first products to reach market. Delivery systems being improved. (BCC research)  Stem cells, cardiology, bone and joint, skin applications are also in forefront of regenerative medicine.
<b>Bioinformatics</b>	Data analysis and advanced computing in biological research.	Projected to exceed \$1.5 billion by 2005. (NES research)	Increasing automation in experiments, data glut, interest in in silico biology. Intersection with IT sector.
<b>Ag-Bio / Food</b>	Agriculture R&D; plant and animal genetics; agri- products processing.	Top 10 global AG-Biotech companies had global revenues of \$22 billion in 2002, 4% increase over 2001.	New varieties of plants being brought on the market and acreage of GM crops increasing annually. Functional foods increasingly accepted globally.

### Related sub-sector of interest:

Sub-sector	Technology/ Product	Growth	Issues, Drivers
<b>Laboratory products</b>	Chromatography, electrophoresis, cell culture incubators, centrifuges Media, Sera and reagents	1996: \$1.75 B; 2001: \$2.17 B Filters 37% growth; Bioseparations 31% growth over next five years (Source: NES reports) U.S. market for media, sera and reagents is expected to be \$915.6 million in 2003. It is further expected to grow at an AAGR (avg annual growth rate) of 13.1% and reach \$1.7 billion by 2008.	Increased biopharmaceutical manufacturing demand with more mAB product approvals. Biomanufacturing is increasing and revolution in cell culture techniques is taking the research to commercial scale processes. (BCC reports.)

<sup>20</sup> “Economic Contributions of the Biotech Industry to the U.S. Economy,” report prepared by Ernst & Young for the Biotechnology Industry Organization (BIO), (accessed at [www.bio.org](http://www.bio.org)). May 2000.

## Glossary

<b>ADMET</b>	acronym for parameters used to understand drug behaviour in a living system Absorption, Distribution (among the tissues), Metabolism, Excretion and Toxicology
<b>Antisense</b>	A nucleic acid sequence that is complementary to the coding sequence of DNA or mRNA.
<b>Bioinformatics</b>	The use of extensive computerized databases to solve information problems in the biological sciences. These databases generally contain protein and nucleic acid sequences, genomes, etc. Bioinformatics also encompasses computer techniques such as 3-D molecular modeling, statistical database analysis, data mining etc.
<b>Cellular</b>	pertaining to the functioning of single cells or cell types that make up a particular tissue
<b>Chromatography</b>	A process in which a chemical mixture carried by a liquid or gas is separated into components as a result of differential distribution of the solutes as they flow around or over a stationary liquid or solid phase
<b>Electrophoresis</b>	A method of separating large molecules (such as DNA fragments or proteins) from a mixture of similar molecules. An electric current is passed through a medium containing the mixture, and each kind of molecule travels through the medium at a different rate, depending on its electrical charge and size. Separation is based on these differences. Agarose and acrylamide gels are the media commonly used for electrophoresis of proteins and nucleic acids
<b>Gene sequencing</b>	The process of determining the sequence of nucleotides in a particular piece of DNA. Also called DNA sequencing
<b>Gene Therapy</b>	Treatment that alters genes (the basic units of heredity found in all cells in the body). In early studies of gene therapy for cancer, researchers were trying to improve the body's natural ability to fight the disease or to make the tumor more sensitive to other kinds of therapy. This treatment may involve the addition of a functional gene or group of genes to a cell by gene insertion to correct a hereditary disease.
<b>Genomics</b>	The identification and functional characterization of genes.
<b>In silico biology</b>	The use of computational algorithms to create virtual systems that emulate molecular pathways, entire cells, or more complex living systems. The use of computers to simulate or analyze a biological experiment.
<b>Metabolomics</b>	The study of the whole metabolism of an organism.
<b>Microbiology</b>	A branch of biology dealing especially with microscopic forms of life
<b>Molecular components</b>	Individual macromolecules of cellular mechanisms are proteins, glycoproteins, lipids and sugars.
<b>Monoclonal AntiBody (mAB)</b>	Highly specific, purified antibody that is derived from only one clone of cells and recognizes only one antigen

<b>Phage display</b>	A technique in which phage are engineered to fuse a foreign peptide or protein with their capsid (surface) proteins and hence display it on their cell surfaces. The immobilized phage may then be used as a screen to see what ligands bind to the expressed fusion protein exhibited (displayed) on the phage surface
<b>Pharmacogenomics</b>	Pharmacogenomics is the study of the stratification of the pharmacological response to a drug by a population based on the genetic variation of that population.
<b>Proteomics</b>	The study of gene expression at the protein level, by the identification and characterization of proteins present in a biological sample.
<b>Recombinant DNA (rDNA)</b>	A combination of DNA molecules of different origin that are joined using recombinant DNA technologies.
<b>Subcellular</b>	Below the cellular level.
<b>SNPs</b>	SNP -- pronounced "snip" -- is short for "single nucleotide polymorphism". A SNP is a place in the genetic code where DNA differs from one person to the next by a single letter. These slight genetic variations between human beings may predispose some people to disease and explain why some respond better to certain drugs. See also pharmacogenomics.
<b>Virology</b>	Study of viruses