

“We’ve discovered the secret of life”

Francis Crick
February 28, 1953

Fifty years ago, James Watson, Francis Crick and Rosalind Franklin discovered the double helix structure of DNA, setting in motion a new way to develop medicine.

It would take another 30 years before the first biotech drug was introduced and begin what economists call....

The Biotech Age

(2000-2025)

Biotechnology v. Pharmaceutical

What is Pharmaceutical Technology?

The study and development of compounds discovered to promote life.

What is Genetics?

The study of DNA and its role in heredity and cell function.

What is Proteomics?

The study of plant, animal and human proteins, their functional roles and their relationships with genes.

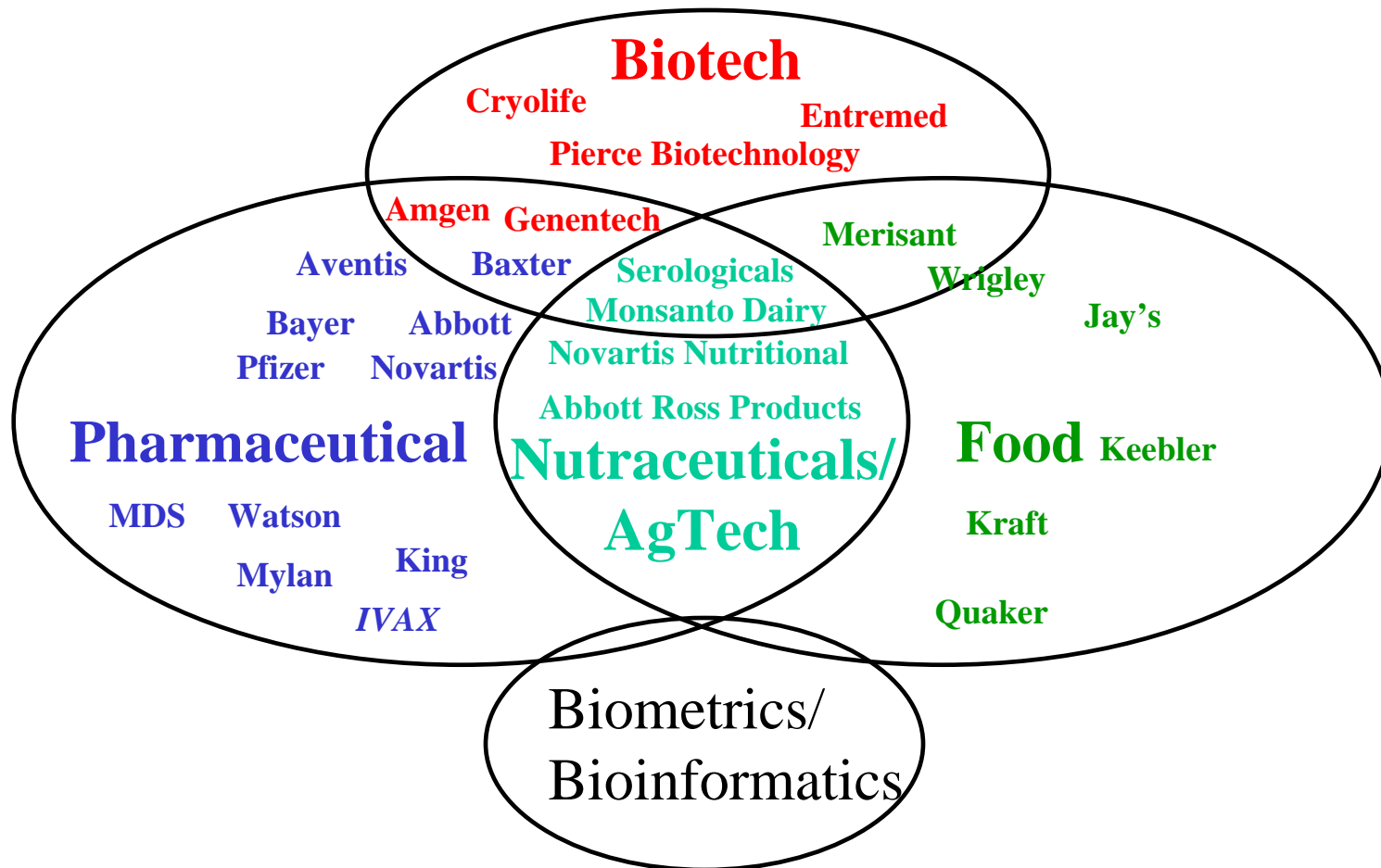
What is Biotechnology?

The study and development of biological products from the information gathered in Genetics.

What is Life Science?

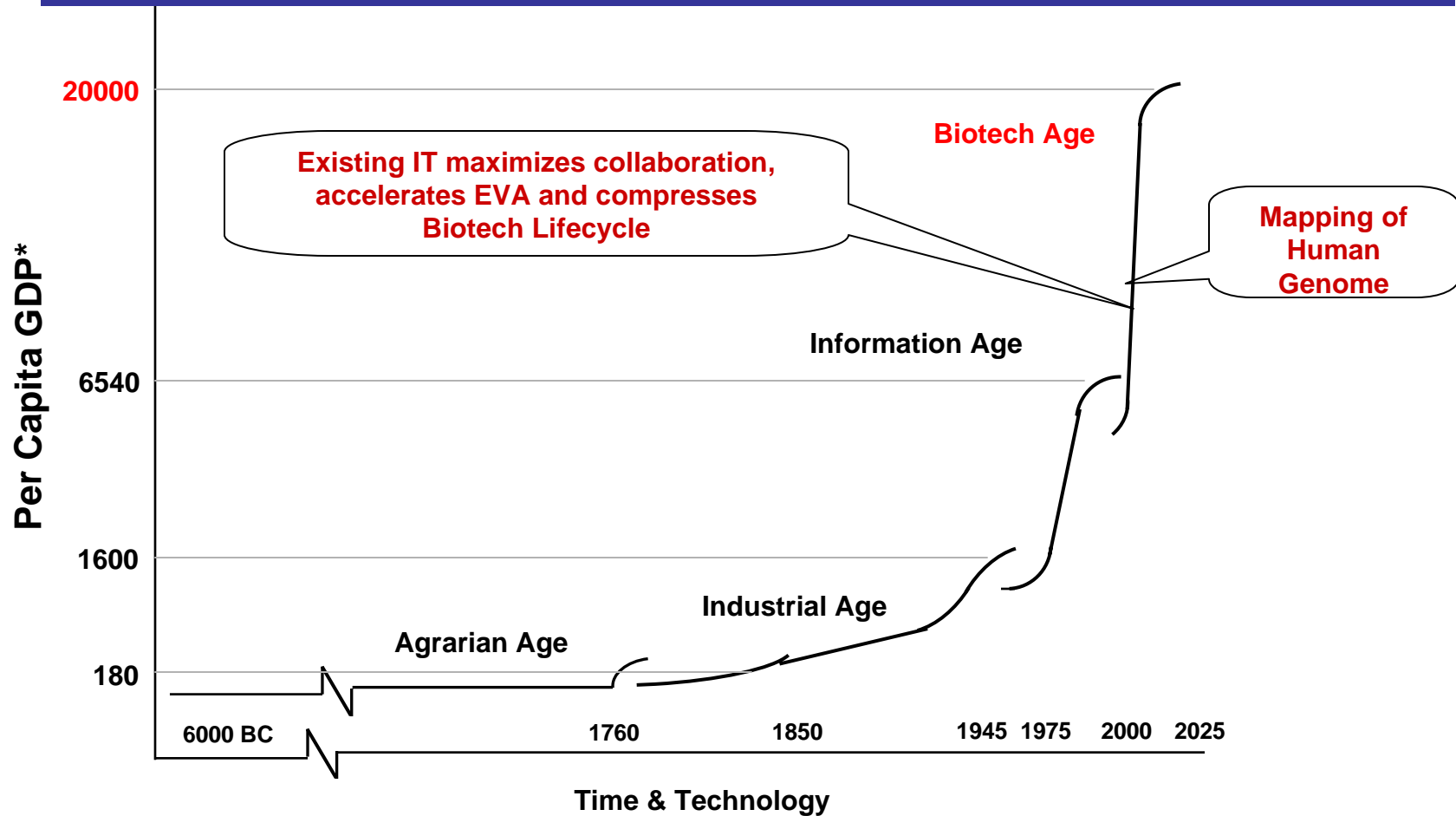
The branch of science concerned with genes and genetic structures affecting, food, animal and human health.

2004 Life Science Strategic Approach



2000-2025

The Biotech Age will create unprecedented EVA



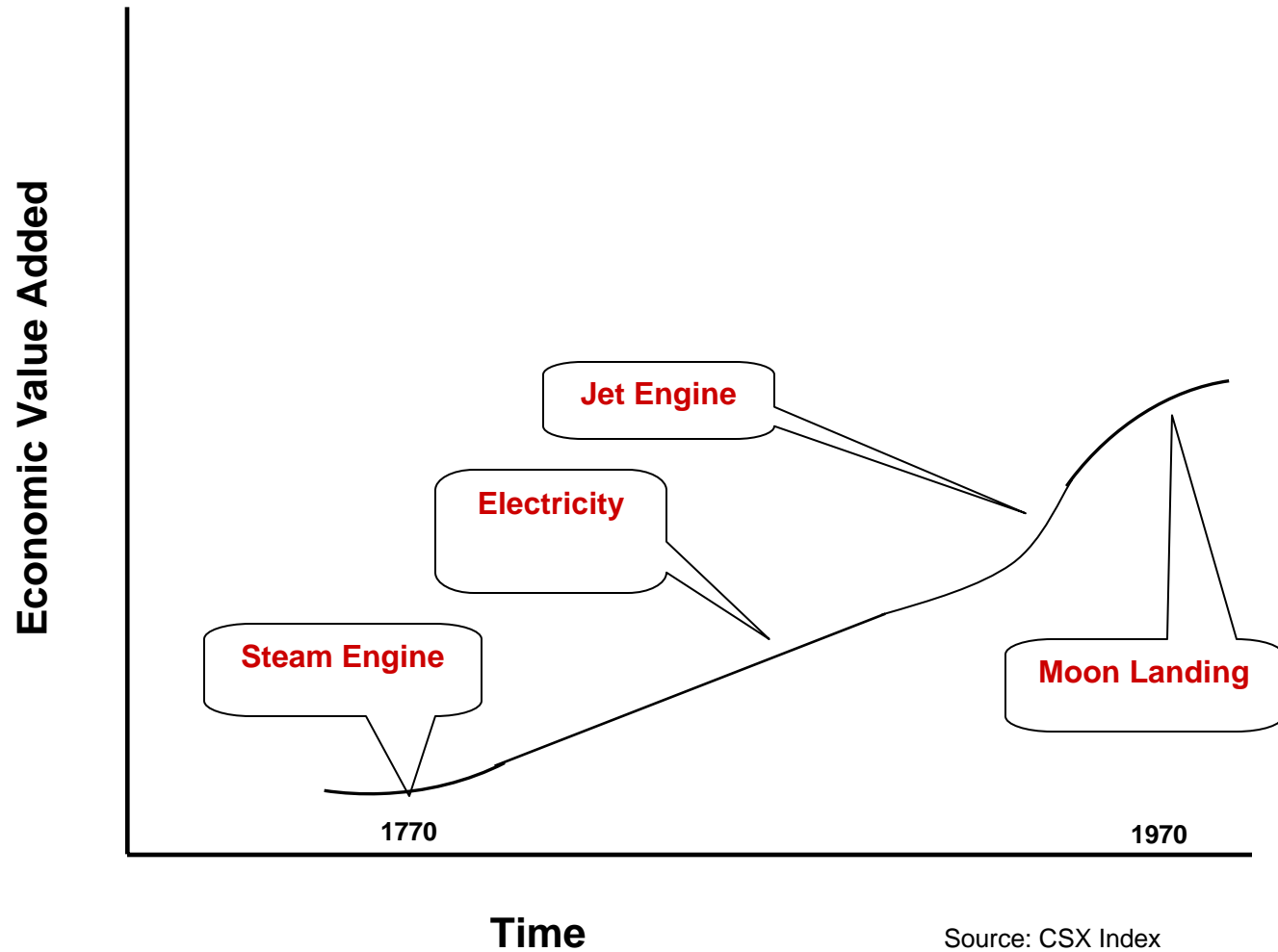
*1996 dollars U.S.

Source: J. Bradford DeLong, Estimating World GDP, 1 Million BC- Present
<http://econ161.berkeley.edu>

The Industrial Age

(1770-1970)

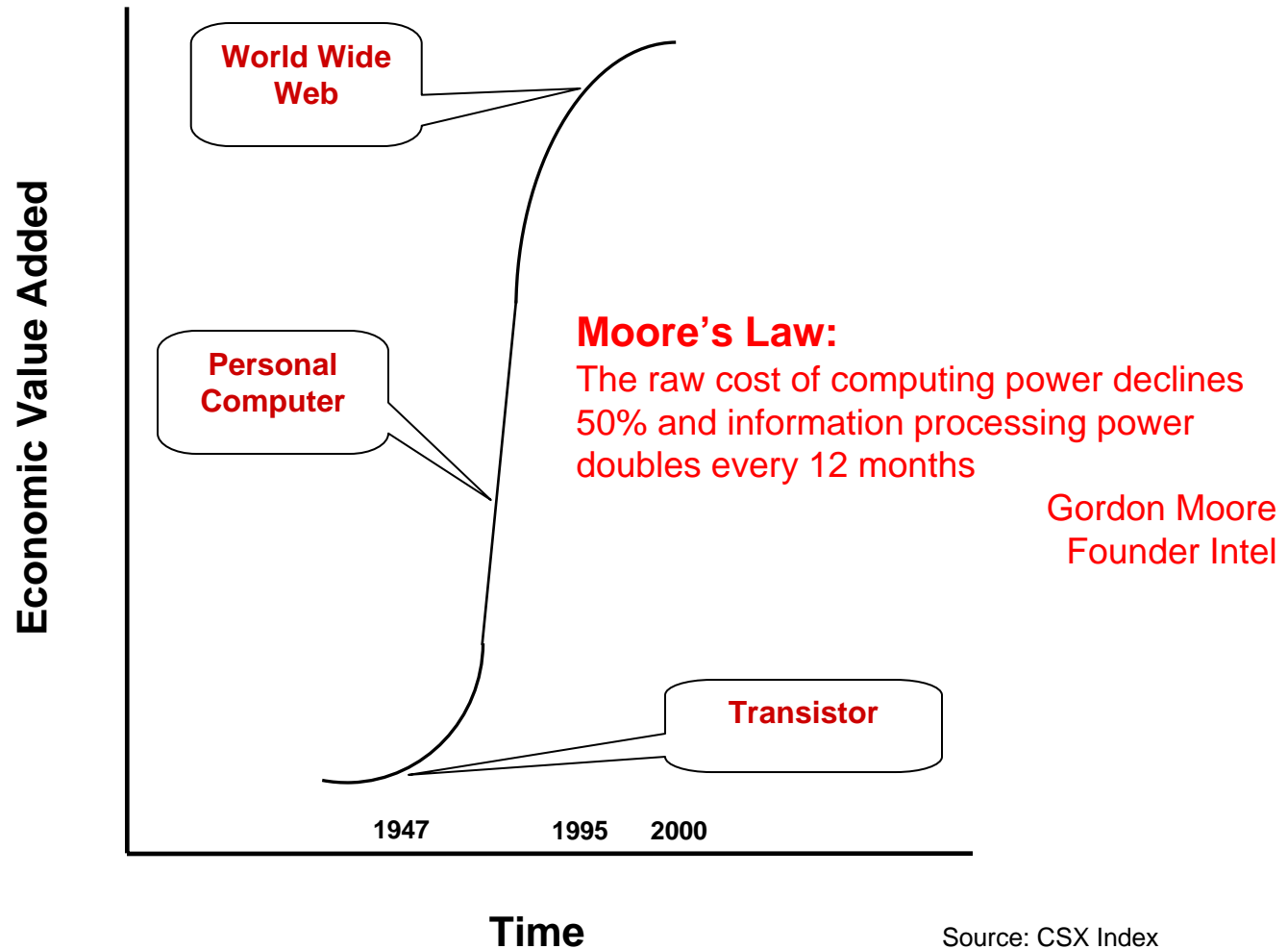
Strategic Inflection Points of the Industrial Age



The Information Age

(1947-2000)

Strategic Inflection Points of the Information Age

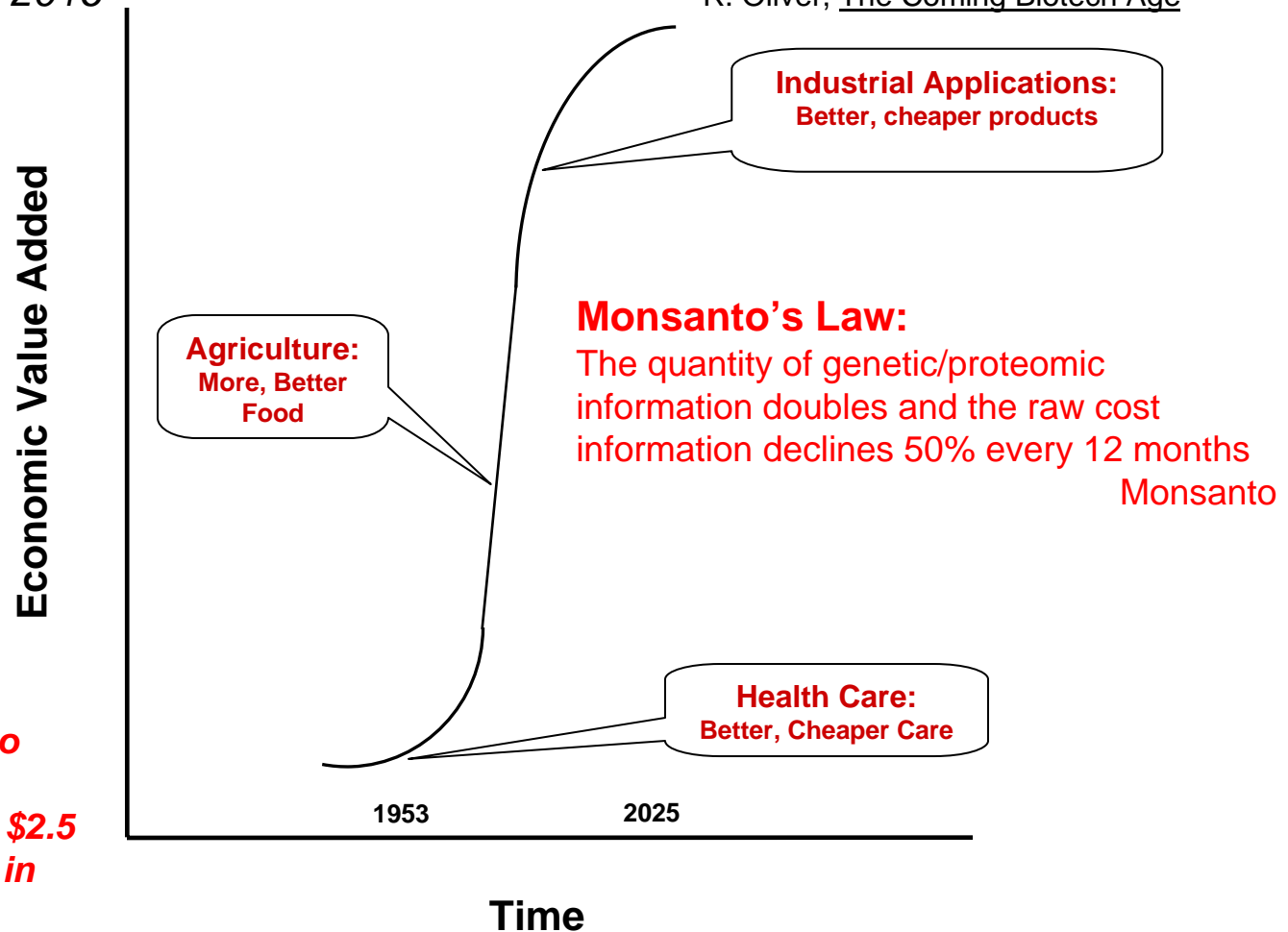


The Pre-Biotech Age

(1953-2000)

Strategic Inflection Points of the Biotech Age

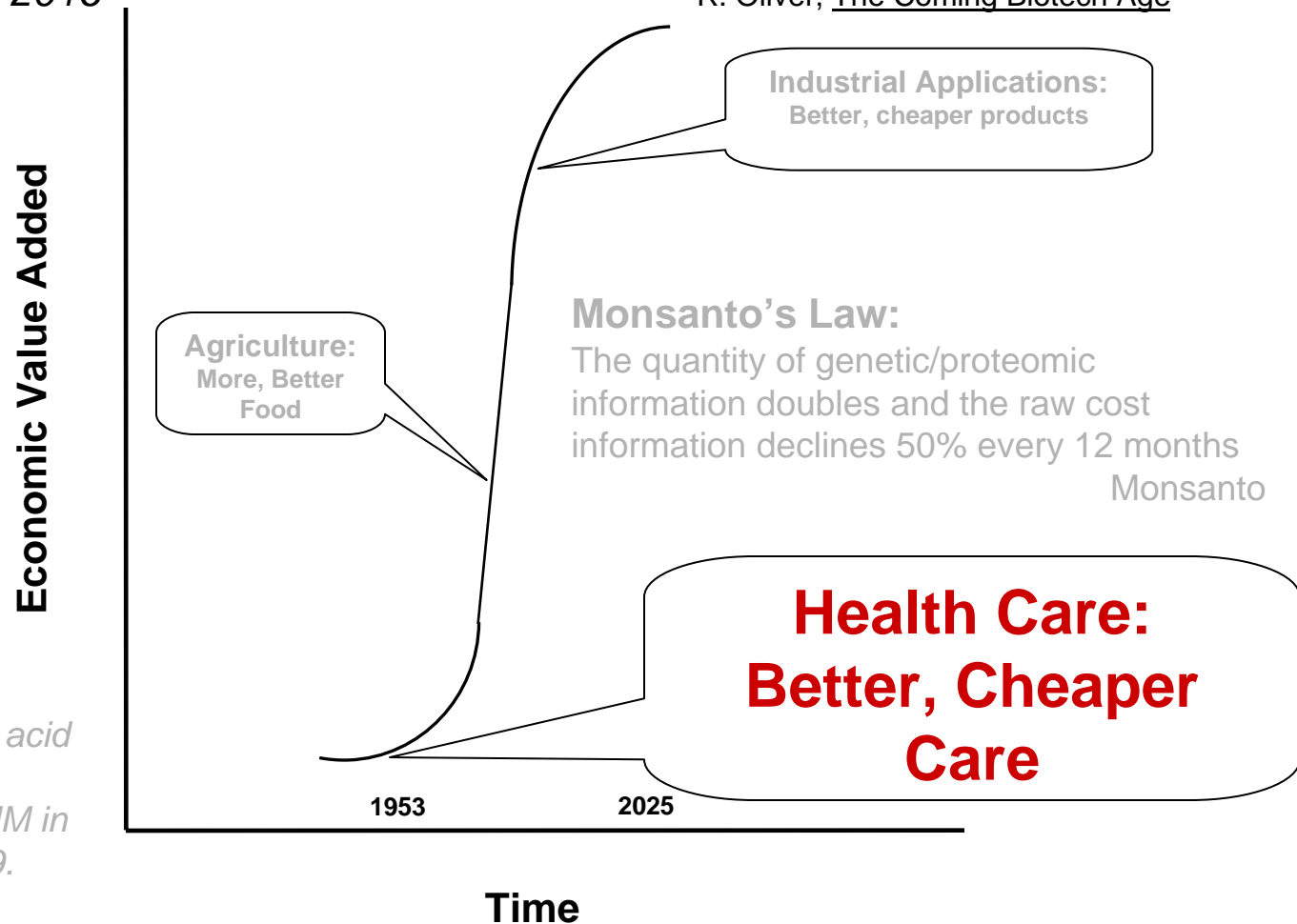
“The stock of biotech knowledge will double monthly by 2015, weekly by 2010 and daily by 2016”
R. Oliver, The Coming Biotech Age



Monsanto's cost to determine the amino acid sequence of a gene dropped from \$2.5 MM in 1974 to \$150 in 1999.

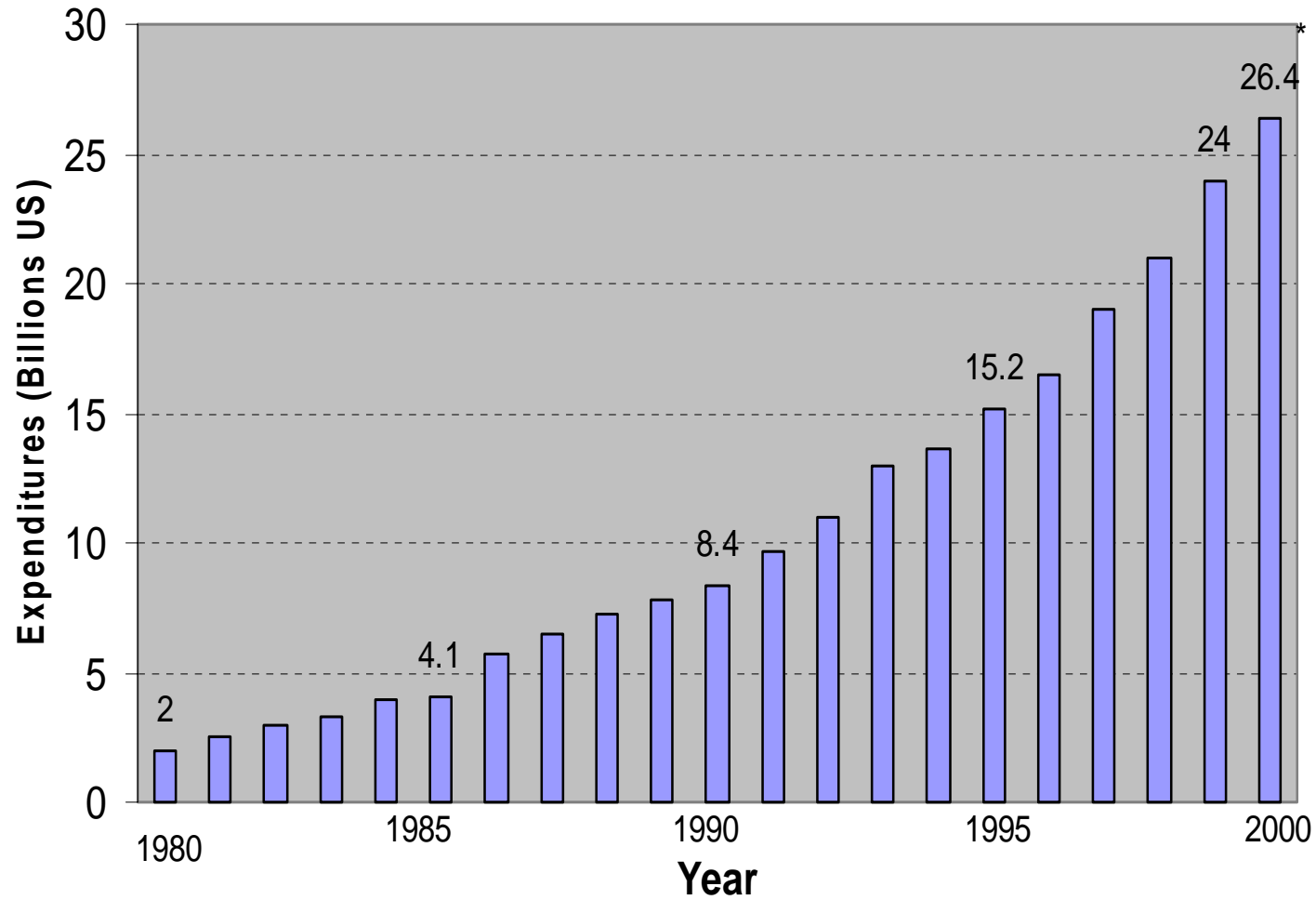
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R&D Investments By Pharma Companies

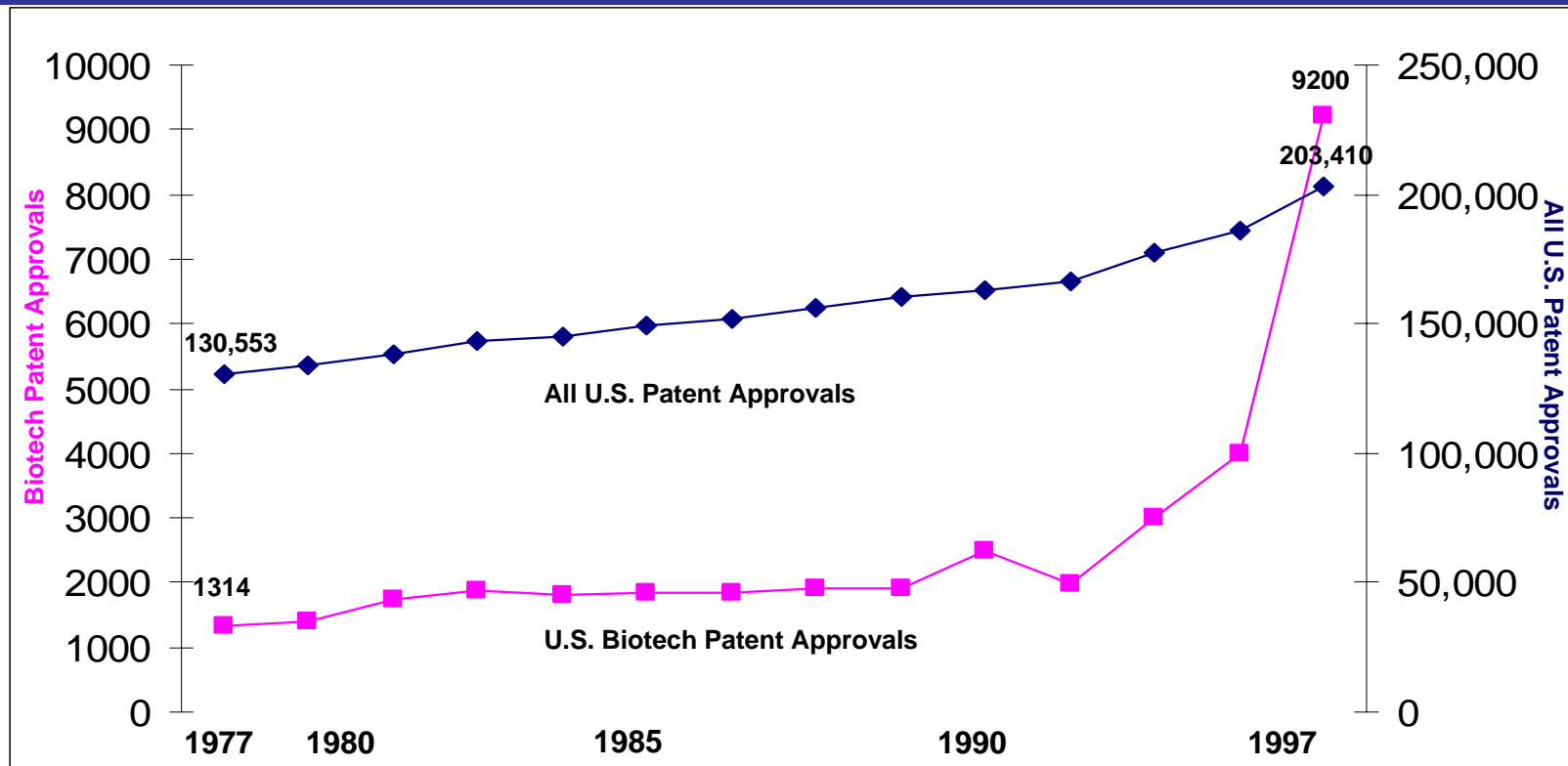


Source: PhRMA Survey 2000

*Estimate

1977-1997

U.S. Biotechnology Patent Approvals increased 700% v. 60% for all U.S. Patents



Source: U.S. Patent & Trademark Office

Biotechnology Firms are by far the most research intensive of all nondefense industries:

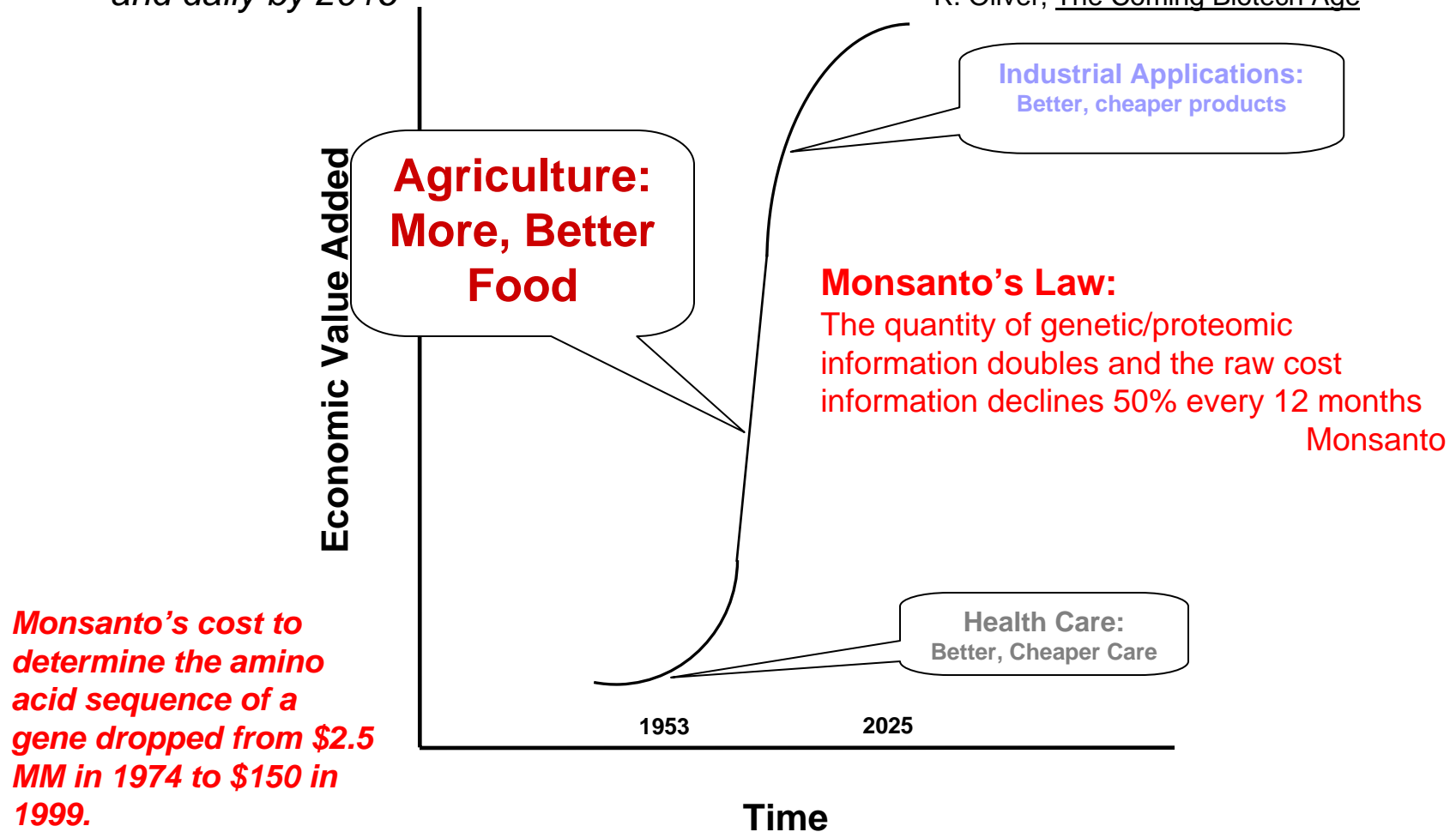
Key Facts (1995):

- Biotech firms spent \$69,000 in R&D per employee in 1995
- Top 5 Biotechs spent \$100,000 per employee
- Top 5 Pharma spent \$40,000 per employee
- Average expenditure for all U.S. corporations was \$7,951

Source: R. Oliver, The Coming Biotech Age

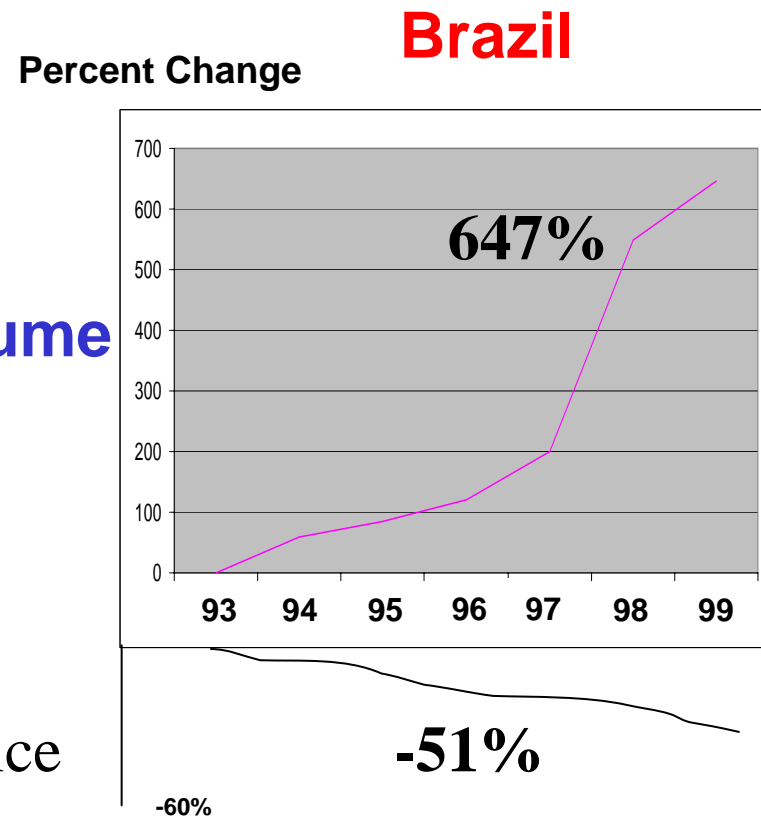
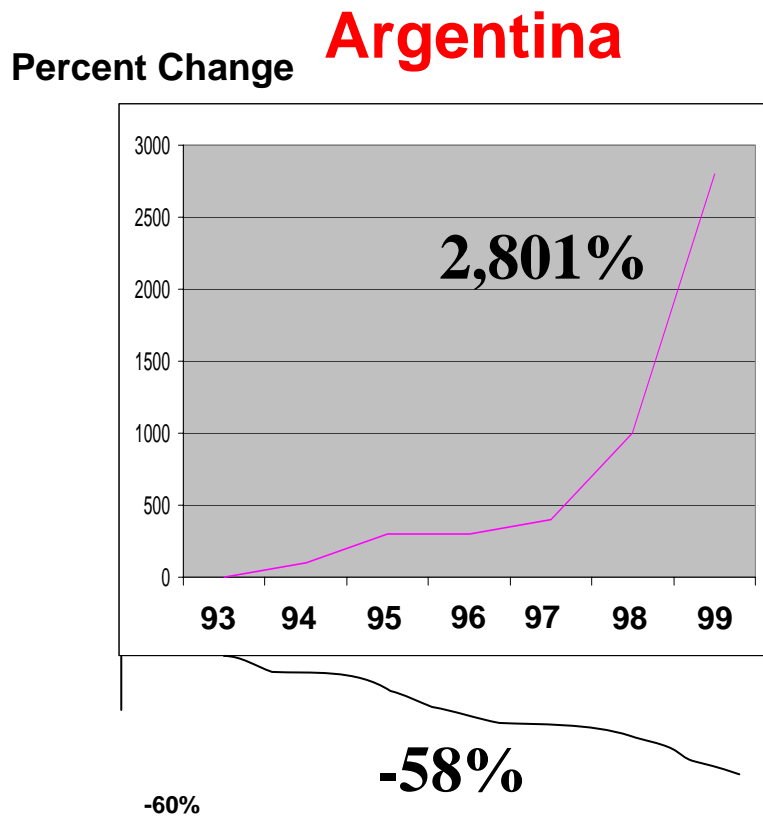
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Impact of Biotech on Agriculture

Yields- by Country- using Roundup-Ready™ seeds (1993-1999)



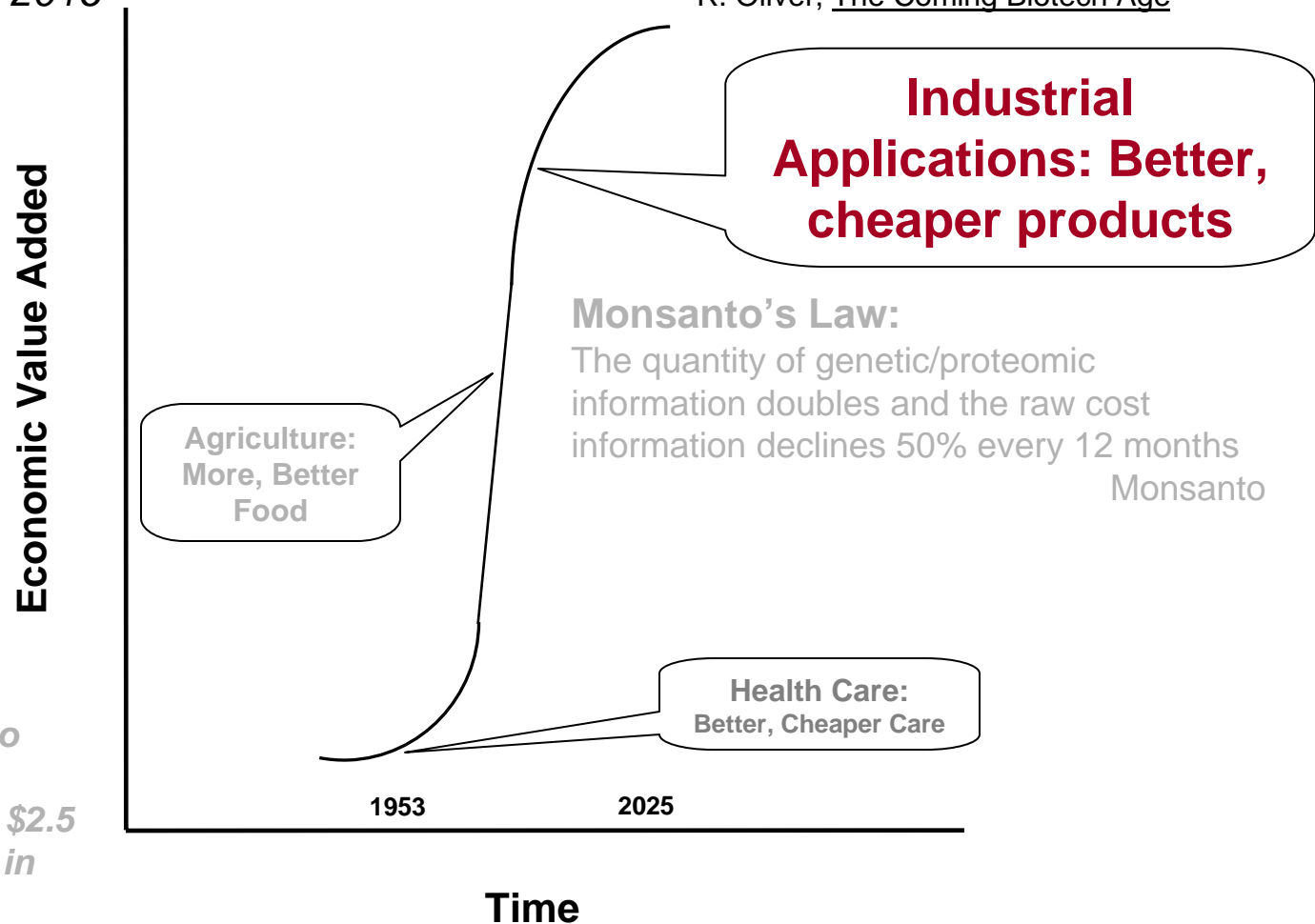
Volume

Price

Source: Monsanto Annual Report 1999

Strategic Inflection Points of the Biotech Age

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Size of Industries Most Affected in The Biotech Age

	Dollars (Billion)	Percent of private-sector GDP
Biotechnology:		
Health Services*	446	6.6
Chemicals and allied products	156	2.3
Environmental services	140	2.1
Agriculture & Forestry	130	2.0
Mining	99	1.5
Bioterials Manufacturing	1,309	19.6
Total	2,280	34.1

Source: U.S. Department of Commerce, Bureau of Economic Analysis

* Note: Health services does not include public sector health care expenditures with amounted to approx. \$330 billion in 1996

Comparison of Biotech Age v. Industrial & Information Ages

Industrial Age- Technology pushed everything to the center

- **Cities were formed around centralized scale economies**
 - New York- Finance
 - Detroit- Automobiles
 - Los Angeles- Entertainment
 - Chicago- Transportation Hub
- **Similarly factories, corporations & countries**
- **Augmented regional barriers to trade- protectionism**

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Information Age- Technology pushed everything to the margins

- **New economic model leveraged information scale economies**
- **Free flow of information augmented decentralization**
- **Regional economies give way to global trade**

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Biotech Age- Technology Transforms Everything Inside Out

- **New 'bioterials' replace conventional materials affecting all products**
- **'Transgenic' crops grow in harshest climates, w/medical payloads (i.e vaccines), eradicating starvation**
- **Genetic therapies discovered to treat/cure cancer, heart disease, obesity, etc.**

“Technological change is but one part of a broader set of forces: an ever increasing conceptualization of our Gross Domestic Product- the substitution, in effect, of ideas for physical matter in the creation of economic value”

Alan Greenspan
Chairman, Federal Reserve
July 10, 1998

The Biotech Age
Snapshot: 2002
A Year of Retrenchment

2002 Defining Events In Life Science

Events

Capital markets enter third depressed year in 2003; risk averse investors play it safe with established, revenue driven companies

Implications

IPOs decline, emerging biotechs scramble for new sources of financing
Publicly traded companies restructure, cutting employees & programs

Deals

Consolidation intensifies

Biotech follows Big Pharma mega mergers to realize research economies of scale, cutting employees & programs

Big Biotech hunts for new products and technologies; rich get richer

Big Pharma pays premium for late-stage drug candidates to fill pipeline

Competition high amongst biotech companies for pharma deals; negotiations take longer as Big Pharma due diligence increases

Products & Technology

250 biotech products in Phase III trials

If half are approved, new launches will increase by more than 70% over the next 3-4 years

Public Policy

Number of FDA approvals decline

Threatens to move more R&D offshore to countries with less regulation

Priority approval times significantly increase

After 21 months without a leader, FDA appoints Mark McClellan as Commissioner

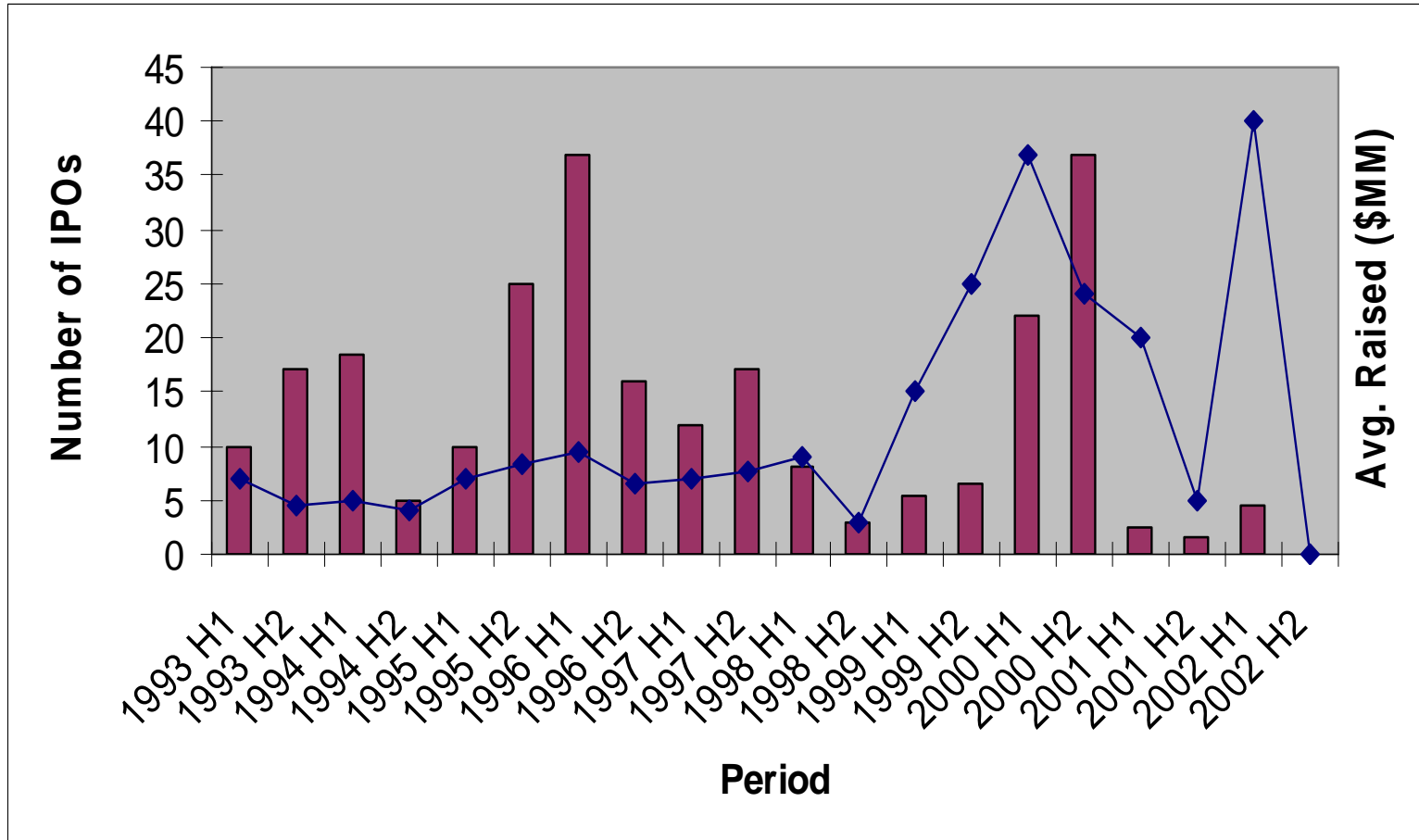
2002 Snapshot: U.S. Biotechnology At A Glance

“It’s a very brutal business. When a drug is pretty much at it’s peak, it just goes away instantly, like switching off a light”

Jean-Pierre Garnier
CEO, Glaxo-SmithKline

- **Withdrawal of risk averse Venture Capital**
- **Significant Penetration by Generics**
- **ImClone Scandal & insider trading effects other public biotechs**
- **FDA approval times increase without appointed Commissioner**
- **Flameout of post-Genomic companies whose model was in gene mining**

U.S. IPOs Over Time



2002 Snapshot: U.S. Biotechnology At A Glance

Public Companies				Industry Total		
	2002	2001	% Change	2002	2001	% Change
Financial	(\$billion)					
Product Sales	21.9	19.1	14.8	24.3	21.4	13.5
Revenues	30.3	26.4	14.8	33.6	29.6	13.5
R&D Expense	16.3	11.6	40.7	20.5	15.7	30.8
Net Income	9.4	4.6	102.3	11.6	6.8	71.2
Industry	(\$billion)					
Market Capitalization	189.5	290.4	-34.7			
Total financings	6.5	5.5	17.9	8.6	7.9	9.5
Number of IPOs	4	4	0	4	4	0
Number of companies	318	342	-7	1466	1457	0.6
Employees	142,900	142,800	0.1	194,600	193,000	0.8

U.S. Biotech: 2002 Financial Highlights by Region

Region	Number of Public Companies	Number of Employees	Market Cap 12/31/02	Revenue	R&D	Net Income	Cash & Short Term Investments	Total Assets
San Francisco Bay Area	62	31,844	49,164	8,994	3,640	1,307	8,774	22,502
	-7%	3%	-37%	17%	4%	25%	-12%	-4%
New England	52	24,447	22,311	4,830	2,836	1,856	6,939	15,988
	-2%	-1%	-44%	15%	17%	48%	-10%	7%
San Diego	28	8,569	12,196	1,647	844	748	3,416	7,543
	-7%	6%	-46%	12%	5%	11%	-9%	8%
New Jersey	24	4,872	5,013	839	528	479	1,310	2,892
	4%	11%	-53%	21%	28%	105%	-20%	-2%
Mid-Atlantic	20	5,984	11,517	1,325	1,943	1,734	3,235	6,104
	0%	6%	-42%	27%	141%	201%	-11%	7%
Southeast	16	3,953	2,317	944	187	139	345	1,274
	-16%	1%	-42%	10%	11%	-406%	-30%	-11%
New York State	15	2,813	3,681	251	390	384	1,077	1,643
	-17%	-5%	-61%	-10%	-31%	-21%	-29%	-27%
Midwest	13	1,156	821	163	119	165	256	426
	-24%	-41%	-48%	-14%	-9%	-30%	-35%	-37%
Pacific NW	17	2,417	3,114	332	489	583	855	1,414
	0%	-36%	-89%	-73%	-18%	128%	-57%	-63%
Los Angeles/Orange County	13	27,091	66,521	7,249	4,281	1,439	5,261	27,472
	-7%	8%	0%	31%	309%	-218%	54%	185%
North Carolina	14	23,388	5,167	2,586	176	9	1,215	3,828
	0%	-5%	-25%	9%	-33%	-97%	8%	19%
Total	318	142,878.0	189,496.0	30,265.0	16,271.0	9,378.0	35,082.0	95,688.0
	-7%	0%	-35%	15%	41%	102%	-9%	20%

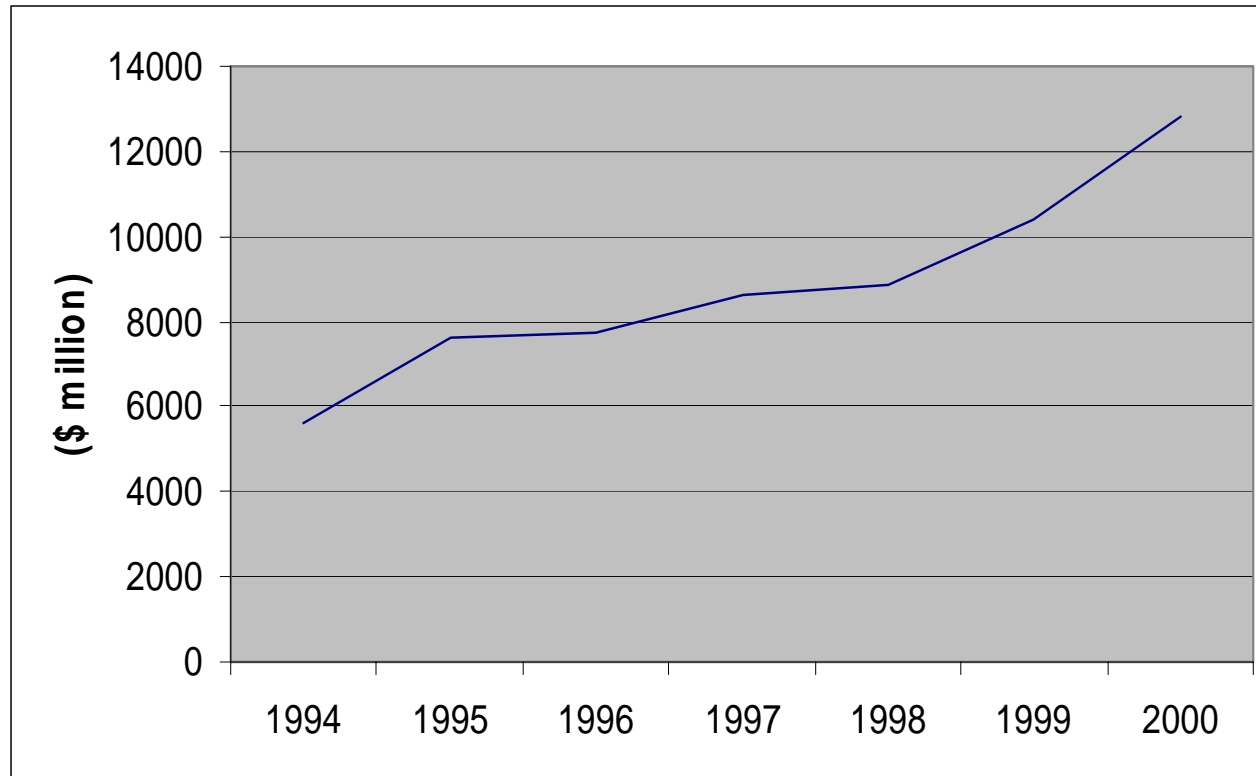
Note: Changes in R&D and Net Income in Los Angeles/Orange County and Mid-Atlantic are due to write-offs for acquired in-process R&D by Amgen and Medimmune related to their acquisitions.

Source: Ernst & Young

2002 Snapshot: U.S. Big Biotech v. Big Pharma

	Revenue (\$MM)	Employees	Revenue per Employee (\$M)	R&D Expense (\$MM)	R&D Expense per Employee (\$M)	R&D Expense as % of Revenue	Net Income (\$MM)	Market Cap 12-31-02	Market Cap 12-31-03	% Change
Biotech										
Amgen	5,523	10,100	547	1,117	111	20	1,600	62,217	80,690	29.69
Genentech	2,618	5,252	498	623	119	24	64	17,067	48,310	183.06
Genzyme	1,329	5,600	237	308	55	23	-13	6,477	11,200	72.92
Chiron	1,172	4,044	290	326	81	28	226	7,073	10,240	44.78
Biogen	1,148	2,633	436	368	140	32	199	5,972	NA	NA
Medimmune	848	1,605	528	144	90	17	81	6,820	6,070	-11.00
Gilead Sciences	467	1,250	373	135	108	29	72	6,687	11,730	75.41
Biovail	788	1,900	415	52	27	7	256	4,146	3,600	-13.17
Weighted Average			429		95	21				54.53
Pharma										
Bristol-Myers Squibb	18,119	44,000	412	2,218	50	12	2,235	44,843	57,020	27.15
Eli Lilly	11,078	43,700	253	2,149	49	19	2,792	71,334	78,750	10.40
Johnson & Johnson	36,298	108,300	335	3,957	37	11	6,786	159,550	153,540	-3.77
Merck	21,631	60,800	356	2,677	44	12	6,788	127,121	106,300	-16.38
Pfizer	32,373	90,000	360	5,176	58	16	9,126	188,377	278,400	47.79
Weighted Average			345		47	10				13.04

U.S. Generic Industry Total Sales

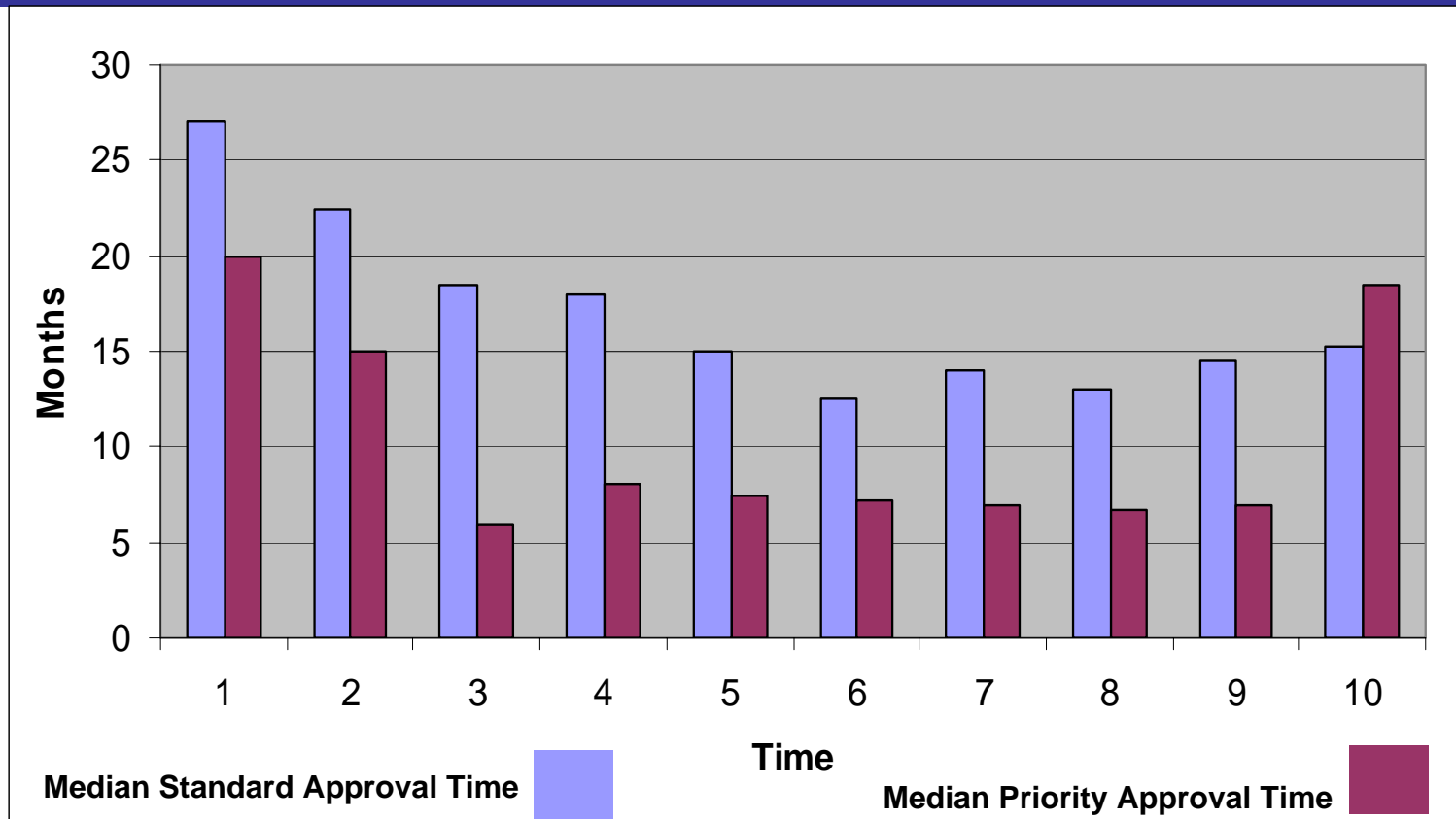


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- **Annualized growth 18%, 1994-2000**
-
- **Between 1997 & 2002, drugs generating \$18 billion came off patent**
-
- **Generics today supply approx. 50% of prescriptions filled**
-
- **Biogenerics pending FDA approval**

Source: PHRMA Survey 2000

FDA Approval Times for all NDAs Increase Significantly

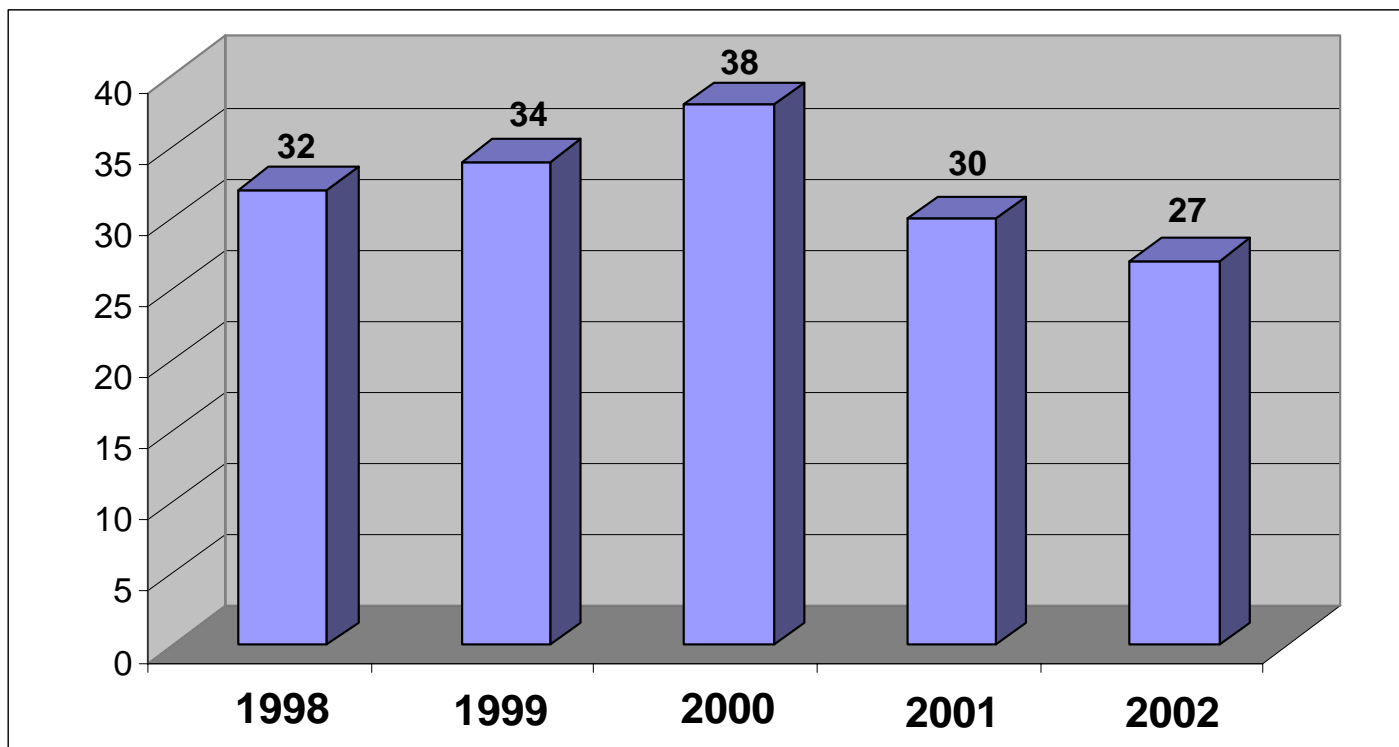
Priority Approval Times Triple....



Source: Ernst & Young

....While Number of Approvals Steadily Declined

Annual New Drug Approvals



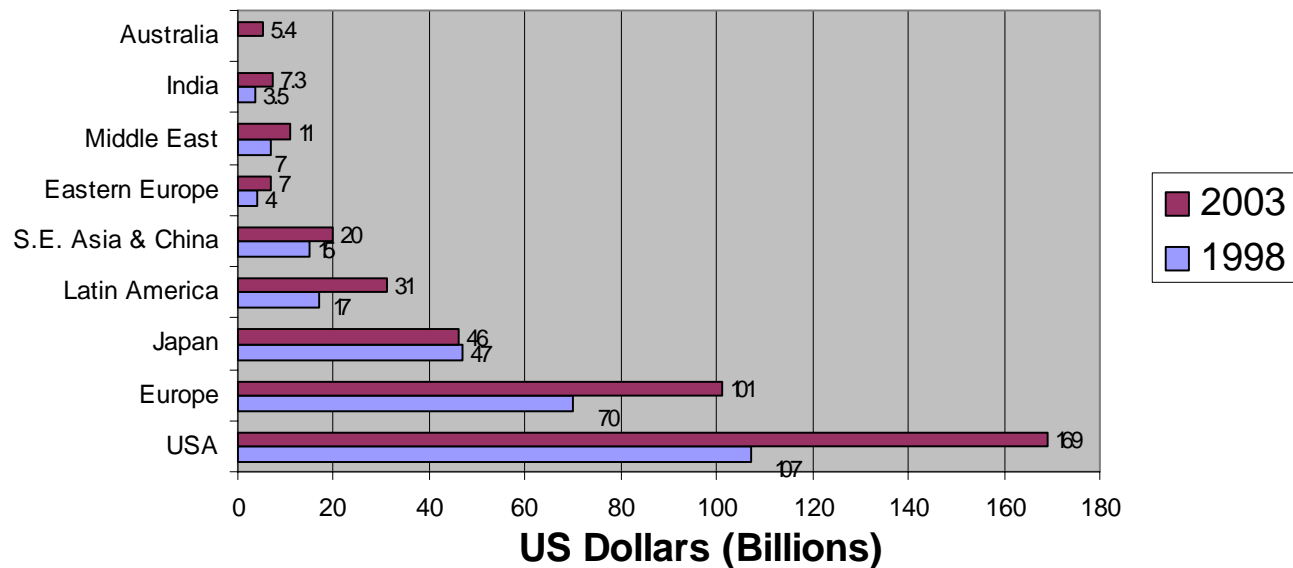
Source: Food and Drug Administration

“The negative technology values now so prevalent in the industry are likely to disappear by 2004 and beyond providing investors with exceptional opportunities...This will follow the painful triage now underway.”

Frederick Frank
Vice Chairman
Lehman Brothers

-speaking specifically of the state of the biotechnology industry, 2003

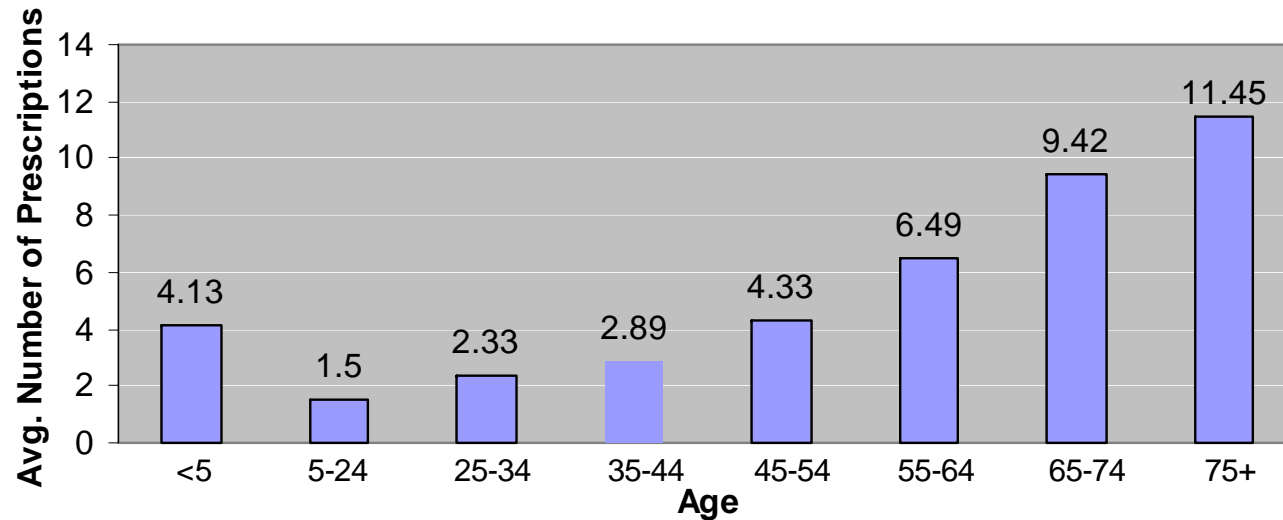
Top 9 Global Markets for Pharma/Biotech



The 9 largest pharmaceutical markets account for 84% of worldwide sales.

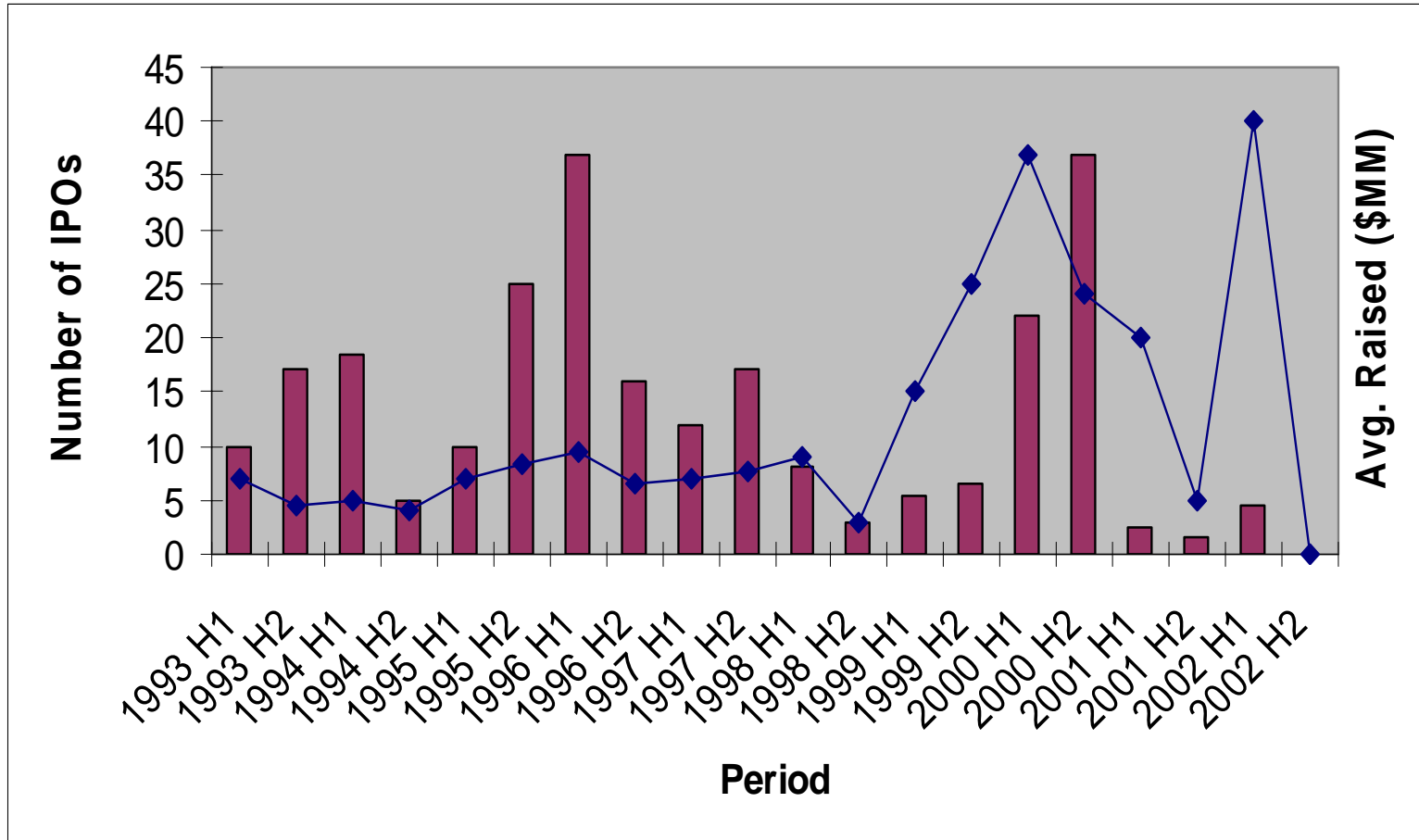
Source: IMS Health 1998

Annual Prescriptions by Age

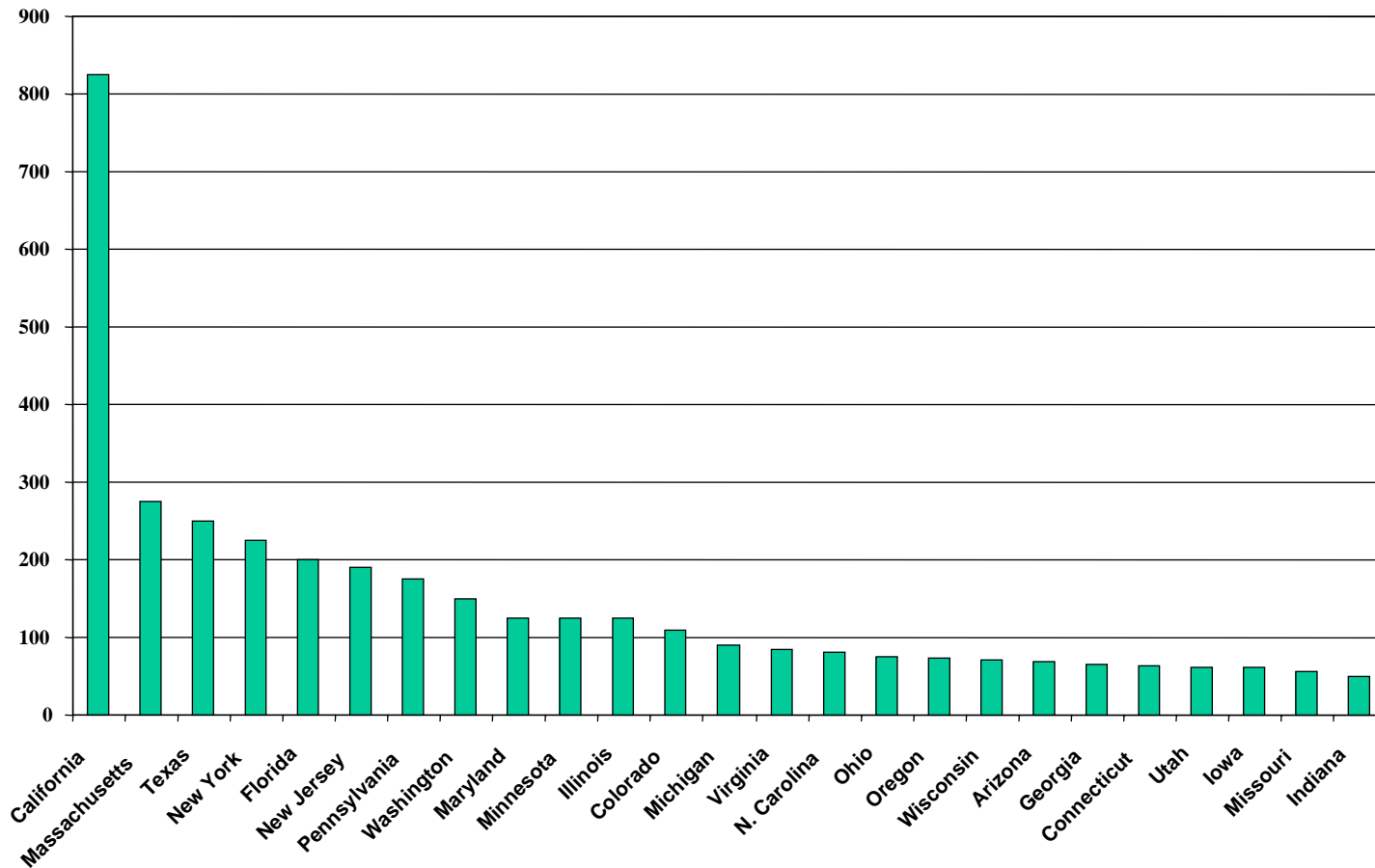


- The over-65 population will grow 16% annually from 1997 through 2010.
- The over-65 population is forecasted to rise from 380 million in 1997 to over 690 million by 2025.
- The over-65 population represents 15% of the total U.S. population, but account for over 33% of total healthcare expenditures.
- **By 2025, total expenditures for Americans over 65 will require 66% of the entire U.S. allotment.**
.....*Federal gov't programs cannot support such an allocation.*
- Congress passes FDAMA to accelerate new drug approval process.

U.S. IPOs Over Time



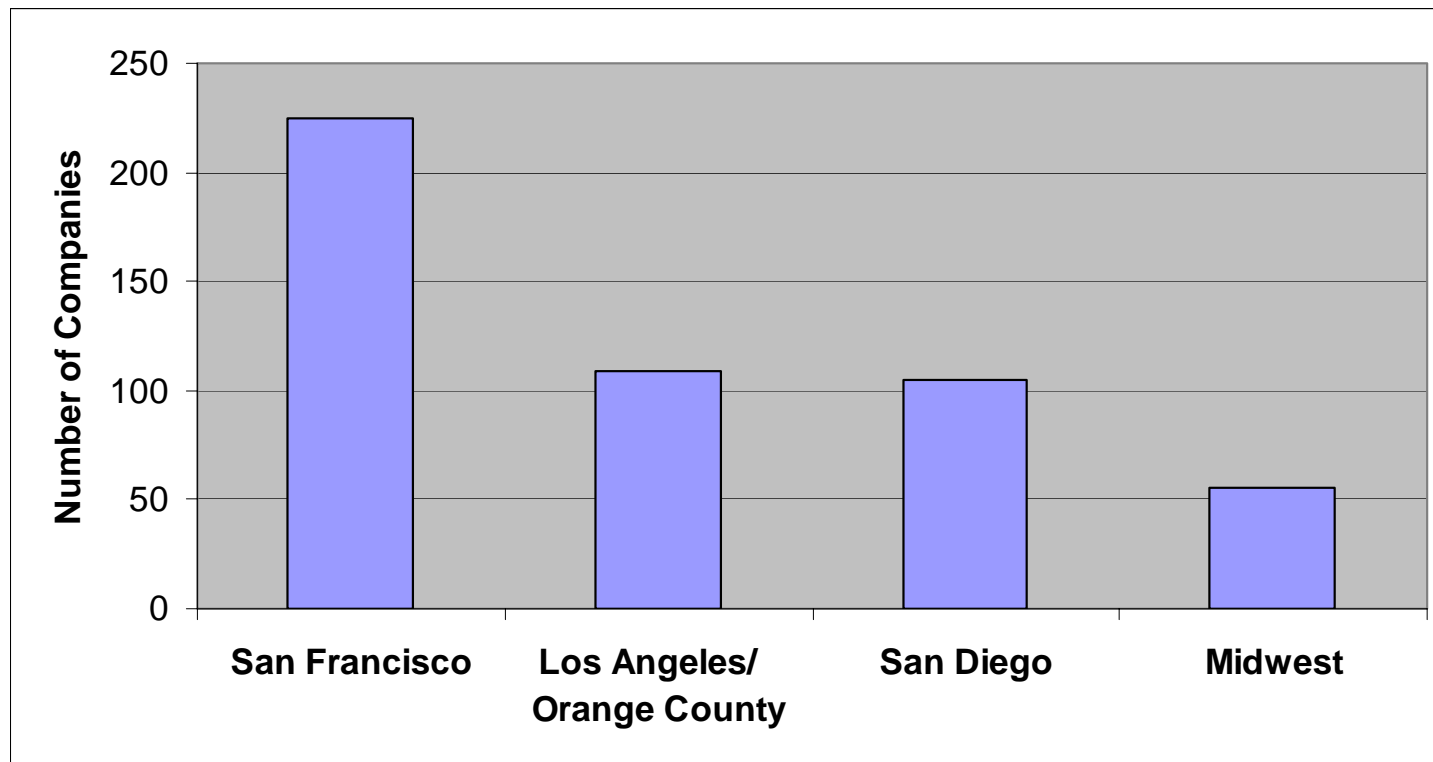
Top 25 States Ranked by Number of Biotech Companies (1999)



Source: From Alchemy to IPO, Roth

Demographic of California Biotech Companies

(with comparison to Midwest)



Source: Ernst & Young

Research & Development- San Francisco

Universities in the San Francisco Region:

- Conduct more than \$1.4 billion in research annually.
 - \$900 million of it is Life Science.
 - \$803 million from NIH in 2001 alone.
 - 75% or \$560 million to UCSF, Berkeley & Stanford.
- Received 1,345 patents in 1999.
 - 38% of all Life Science patents in the state.

Source: Bay Bio

Venture Capital- 2002

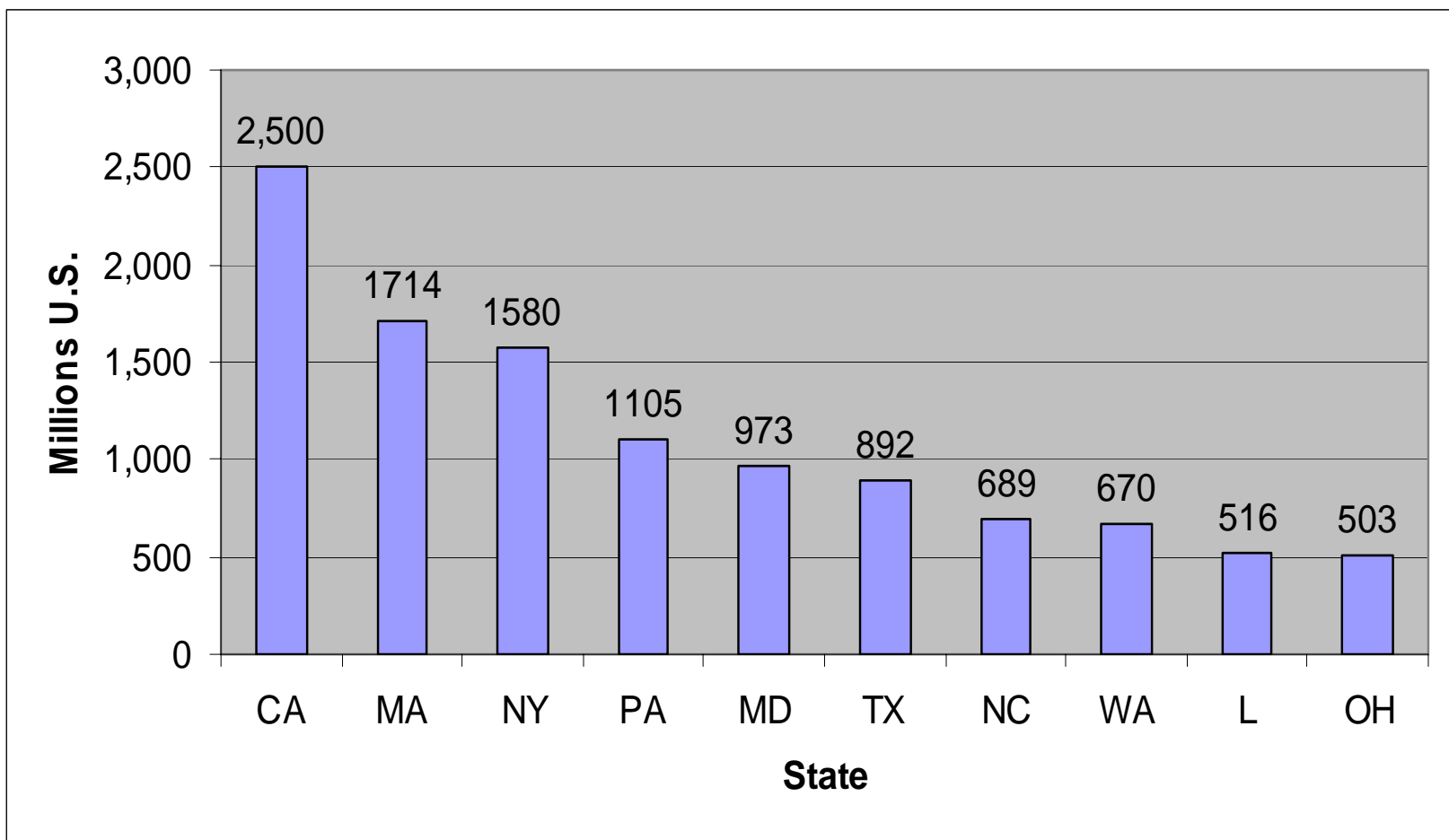
“ Between 1998 and 2001, Bay Area biopharma companies conducted 31 IPOs as compared to the next highest IPOs of 10 and 8, respectively for the San Diego and Seattle regions.” Brookings Institute

The Bay Area Dominates the Venture Capital Market:

- The most V.C. firms in the U.S.- 21
 - #2 Boston has 10.
- 33% of all deals in the U.S.
- 40% of all venture capital investment in the U.S.
- 77% of all venture capital investment in California.
- 570% increase in investments between 1995-2001.

Source: Bay Bio Report, 2003

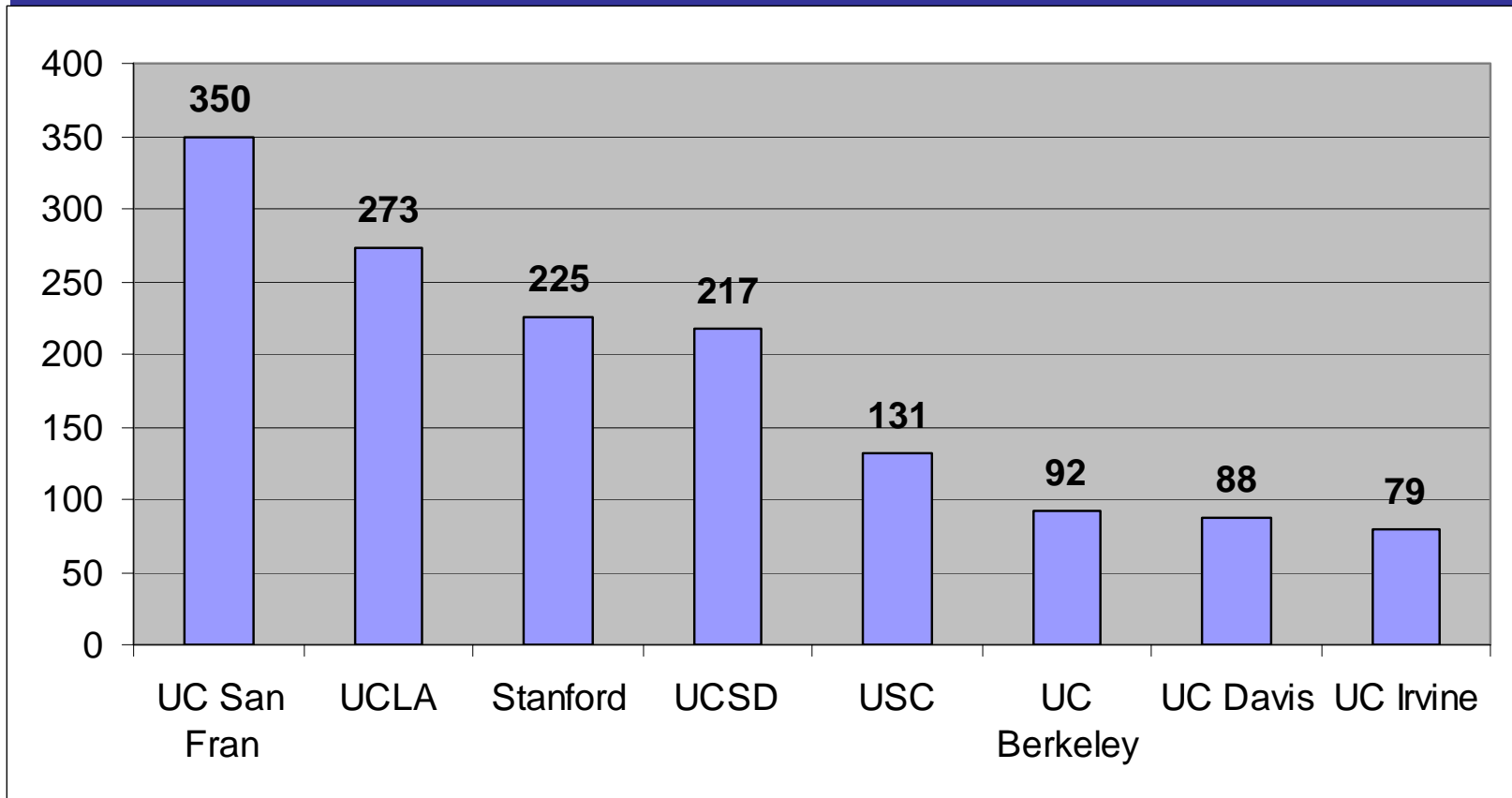
NIH Funding By State



Source: NIH

NIH Funding- California Universities

4 of the top 8 are in the Bay Area - 2002



Source: NIH - 2003

California University Spin-Off Companies

Approx. 50% are in the Bay Area

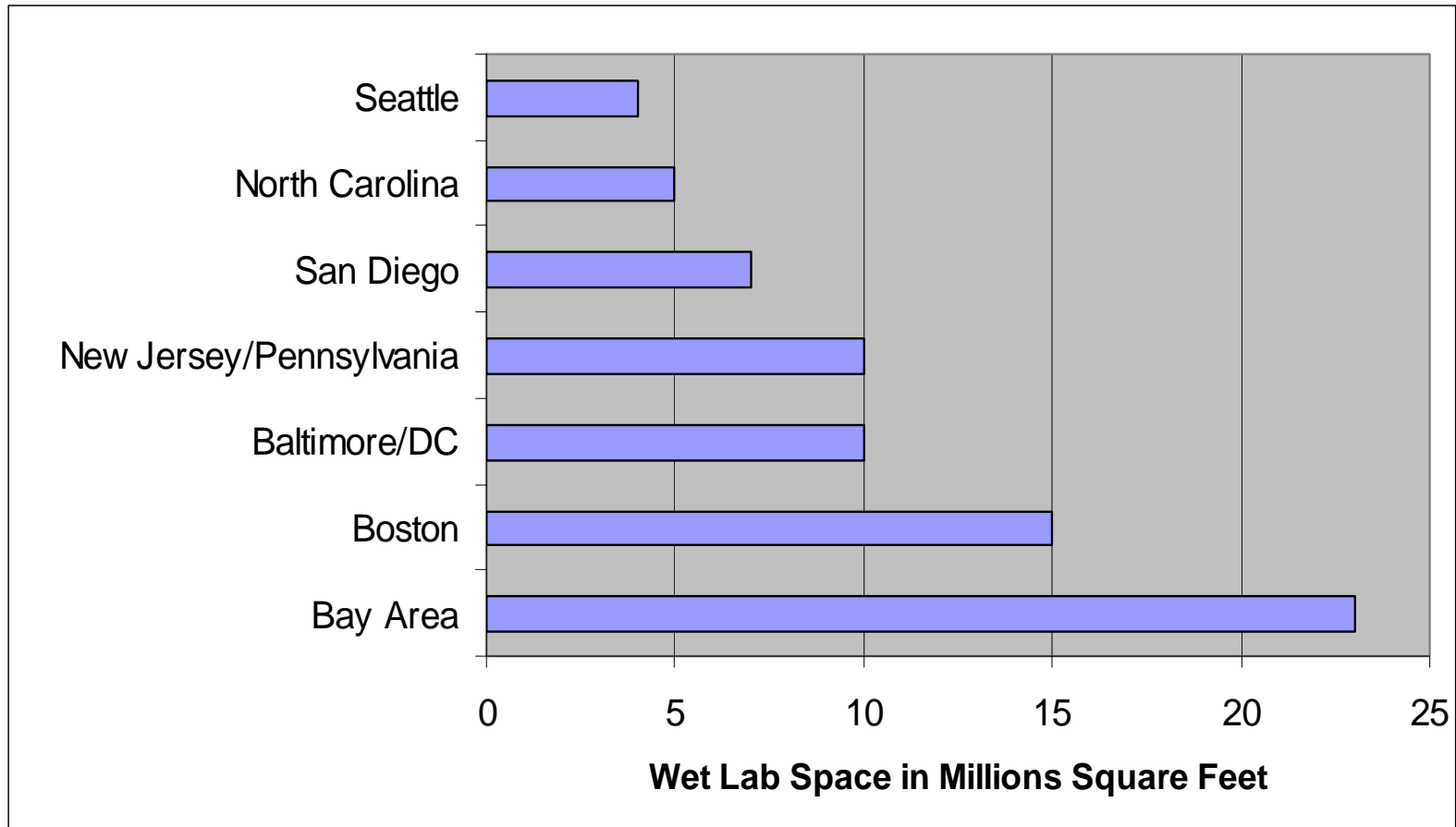
Institution	Biomedical Companies
Stanford University	94
UC San Diego	63
UC San Francisco	60
UC Berkeley	39
The Scripps Research Institute	33
Caltech	24
UC Davis	18
UC Los Angeles	18
The Salk Institute	16
UC Irvine	9
Lawrence Berkeley/Lawrence Livermore National Labs	7
The Burnham Institute	7
UC Riverside	5
UC Santa Barbara	5
UC Santa Cruz	3
City of Hope	1
Bay Area Total	200
Total California	402

Biotech projected growth:

Demand for Antibody Products			(Grams/Year)				
FDA Status	Disease Indication	Firm	2002	2003	2004	2005	2006
W	Colorectal cancer	Abgenix, Amgen	0	0	0	3.3	24.7
A	Psoriasis	Biogen	0	0.8	2.2	2.7	3
W	Chrohn's disease, MS	Elan, Biogen	0	0	0	25	50
W	Colon cancer	Genentech	0	0	466	1,305	2,714
W	Non-Hodgkin's Lymphoma (NHL)	Beckman Coulter, GlaxoSmithKline, Amersham	0	0.3	0.7	1.4	1.9
A	B-Cell chronic lymphocytic leukemia	Ilex	1	1.1	1.4	1.8	2.3
A	Rheumatoid arthritis (RA)	Amgen	180.3	284.8	361.7	397.9	437.7
W	Colorectal cancer	ImClone, Merck	0	0	160	320	640
A	Breast cancer	Genentech	62.4	64.3	71.3	78.5	86.3
A	Rheumatoid arthritis	Abbott, Cambridge Antibody	0	22.7	45.3	71.1	99.6
W	Mucositis	Amgen	0	0	0	0.1	0.2
W	Postoperative glaucoma surgery	Cambridge Antibody Technology	0	0	0	0	0
W	Age-related macular degeneration	Genentech	0	0	0	0	0
W	NHL	Amgen, Immunomedics	0	0	0	0	0
A	Acute myelogenous leukemia	Wyeth	0.04	0.04	0.04	0.04	0.04
W	Osteoporosis	NPS Pharmaceutical	0	0	0	0.1	0.5
W	Psoriasis	Genentech, Xoma, Serono	0	4.3	85.6	154.2	231.2
A	Crohn's disease, RA	Johnson & Johnson, Centocor	220.5	291.1	346.4	412.2	490.5
A	Angioplasty	Lilly	8.4	7.9	7.8	7.8	7.8
A	NHL	Genentech, Idec	368.9	479.5	575.4	707.8	884.8
A	Respiratory syncytial virus	Medimmune	72.9	92.6	116.7	141.2	166.7
A	Allergic asthma	Genentech/Tanox/Novartis	0	18.4	73.4	138	207
A	Acute rejection	Roche	2.1	2.1	2.1	2.1	2.1
A	NHL	Idec/Schering	0.0026	0.0062	0.012	0.0165	0.0215
Total (kg)			917	1,270	2,316	3,770	6,050

Source: Dr. Charles Christy & UBS

Comparative Wet Lab Markets



Source: St. Louis Register, Oct. 2001

In Summary- San Francisco

“In general, the emerging pattern of growth in the Life Sciences suggests that new employment will likely consist of R&D (50%), manufacturing (25%), and commercial, marketing, management and support positions (25%). Given the importance of the Life Sciences to the economy of the Bay Area, it is critical for the supply of skilled labor to meet the cluster’s burgeoning needs.

Considering the long lead times inherent in changing and improving a region’s human capital equation, there are reasons to fear that the requirements of growth will outstrip the available human assets”

Bay Area Life Sciences Strategic Action Plan

2003

In Summary- Biotech

“A Man’s Character Is His Fate.”

Heraclitus

“We talk about gene therapy as if it can change someone’s fate, but you can also change someone’s fate if you pay off their credit card.”

James Watson

In Memoriam: Dolly the Sheep, 1997- 2003
(the first cloned mammal from embryonic stem cells)