JENNIFER A. TEGFELDT, ESQ.

Jennifer holds a degree in Biological Sciences from the University of California, Davis. Following a several year career as an analytical chemist, Jennifer graduated from Pierce Law in 1985 with the goal of practicing intellectual property law. The IP program, back then, was substantially different than now – Jennifer was the only woman in a class of eight men. She served as an editor to "Idea, the Journal of Law and Technology" almost from the beginning of her legal education. She counts among her most important mentors and guides (as do a number of IP students of Pierce Law), the irreplaceable Professor Bob Shaw, who never saw obstacles, only opportunities.

Jennifer was the first alumnus to be appointed law clerk to a judge of the Court of Appeals for the Federal Circuit. Jennifer served as law clerk to Judge Pauline Newman from 1985-1987, and assisted in such proceedings as Pennwalt, Texas Instruments, In re Thorpe, and the FAA air controller cases.

When her clerkship ended in 1987, Jennifer entered private practice with a small boutique patent law practice and was later recruited to join Fitzpatrick, Cella, Harper and Scinto in the firm's Washington D.C. offices. Her practice focused on patent prosecution and enforcement, appeals, trademarks, copyrights, licensing, and opinion work of all types. Jennifer was very active in the Federal Circuit Bar Association, AIPLA, ITC Trial Lawyers Association, American Bar Association, including gaining Delegate status in the ABA's House of Delegates for the Federal Circuit Bar Association, and the American Inns of Court, Giles S. Rich Inn.

In 1994, Jennifer left private practice to join Genzyme Corporation as one of four attorneys supporting the company. Since that time, the legal team has grown to over twenty patent and corporate lawyers. Jennifer maintains a patent practice, while working closely with the corporate legal team in transactional matters, and in leading legal efforts to develop and put in place collaborations. Within the last year, Jennifer has expanded her "Transactional IP" role in taking on a strategic position in the Business Development team for the Therapeutics business unit of Genzyme General, a division and tracking stock of Genzyme Corporation. As Director, Business Initiatives and IP Legal Affairs, she continues to pursue her business knowledge as a logical and necessary component of intellectual property management and corporate growth.

Jennifer lives in the Boston area, and her friends know that when the winter weather breaks, she'll most likely be out on the water exploring the coast in her sailboat.

BIOTECHNOLOGY LICENSING

A VIEW FROM THE INSIDE

ELEVENTH ANNUAL ADVANCED LICENSING INSTITUTE
PIERCE LAW
CONCORD, NEW HAMPSHIRE
JULY 15-19, 2002

Jennifer A. Tegfeldt, Esq.
Director, Business Initiatives and
IP Legal Affairs
Genzyme Corporation
Cambridge, Massachusetts

DISCUSSION POINTS

- THE BUSINESS OF BIOTECHNOLOGY
- FORMS OF COLLABORATION
- DEVELOPING THE PROCESS
- CONTRACTUAL CONSIDERATIONS
- ADDITIONAL THOUGHTS IN CRAFTING A SUCCESSFUL COLLABORATION

I. THE BUSINESS OF LIFE -- BIOTECHNOLOGY

An Historical Perspective

Source : 2002 Biotechnology Industry Association, www.bio.org, Time Line of Biotechnology

800 B.C.	Humans domesticate crops and livestock
4000-2000 B.C.	Production of cheese and fermentation of wine (Sumeria, China and Egypt) Babylonians control date palm breeding by selectively pollinating female trees with pollen from certain male trees
500 B.C.	First antibiotic made of moldy soybean curds to treat boils (China)
A.D. 100	First insecticide made of powdered chrysanthemums (China)
1590-1675	1590 – Janssen invents the microscope 1663 – Hooke discovers the cell 1675 – Leeuwenhoek discovers bacteria
1797	Jenner inoculates a child with a viral vaccine against smallpox
1830-1855	1830 – Proteins discovered 1833 – First enzyme discovered and isolated
1835-1855	Scheiden and Schwann propose that all organisms are made of cells Virchow announces "Every cell arises from a cell"
1859	Darwin publishes the theory of evolution by natural selection
1865	Genetics begins with Austrian monk Gregor Mendel studying garden peas and discovering that genetic traits are pass from parents to offspring in a predictable way – the laws of heredity
1877-1879	1877 – Koch develops a technique for staining and identifying bacteria 1878 – The first centrifuge is developed by Laval 1879 – Fleming discovers chromatin, the rodlike structures in the nucleus that became known as chromosomes
1902-1915	1902 -- The term "immunology" first appears 1906 -- The term "genetics" is introduced 1915 -- Phages, or bacterial viruses, are discovered

1920	Human growth hormone discovered by Evans and Long
1928	Penicillin discovered as an antibiotic by Alexander Fleming
1944	Avery et al. prove DNA carries genetic information
1946	Discovery that genetic material from different viruses can be combined to form a new type of virus, an example of genetic recombination
1949	Pauling shows that sickle cell anemia is a "molecular disease" resulting from a mutation in the protein molecule hemoglobin
1953	"Nature" publishes James Watson and Francis Crick's manuscript describing the double helical structure of DNA
1956	Kornberg discovers the enzyme DNA polymerase I, leading to an understanding of how DNA is replicated
1966	The genetic code is cracked, demonstrating that a sequence of three nucleotide basis (a codon) determines each of 20 amino acids
1969	An enzyme is synthesized in vitro for the first time
1971	First complete synthesis of a gene
1973	Stanley Cohen and Herbert Boyer perfect genetic engineering techniques to cut and past DNA (using restriction enzymes and ligases) and reproduce the new DNA in bacteria
1976	First time the sequence of base pairs for a specific gene is determined (A, C, T, G)
1977-1979	First expression of a human gene in bacteria Recombinant human insulin first produced Human growth hormone first synthesized
1980	U.S. Supreme Court, in Diamond v. Chakrabarty, approves the patenting of genetically engineered life forms
1981	Scientists at Ohio University produce the first transgenic mice
1983	Conception of polymerase chain reaction (PCR), in which heat and enzymes are used to make unlimited copies of genes and gene fragments

1985	Genetic markers found for kidney disease and cystic fibrosis
1986	First genetically engineered vaccine for humans: hepatitis B First anticancer drug through biotechnology: interferon
1988	Harvard molecular geneticists receive first U.S. patent for genetically altered animal – a transgenic mouse ("the onco-mouse")
1990	Human Genome Project – an international effort to map all the genes in the human body – is launched First transgenic dairy cow used to produce human milk proteins for infant formula
1994	First breast cancer gene discovered
1997	First animal cloned from an adult cell: a sheep named Dolly
1998	Embryonic stem cells used to regenerate tissue and create disorders mimicking diseases
2000	Rough draft of the human genome sequence is announced
2001	Scientific journals publish complete human genome sequence

"...anything under the sun that is made by man."
Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980)

- The Possibilities of Biotechnology
  - Agriculture
    - Higher producing and drought and insect resistant plants
    - Better tasting and longer lasting vegetables and fruits
    - Higher productivity animals
  - Therapeutics
    - Gene Therapy
    - Protein Therapies
    - Diagnostics, including genetic testing
    - Improved patient therapy monitoring
    - Cell Therapies
    - Combination Therapies
    - Synergies with "chemical" therapies
  - Discovery
    - Models for disease, cell and animal
    - Screening techniques
  - Manufacture
    - Plant (such as picchia)
    - Insect
    - Mammalian cells (human and CHO)
    - Transgenic animals
  - Environmental uses
    - Hazardous waste clean-up

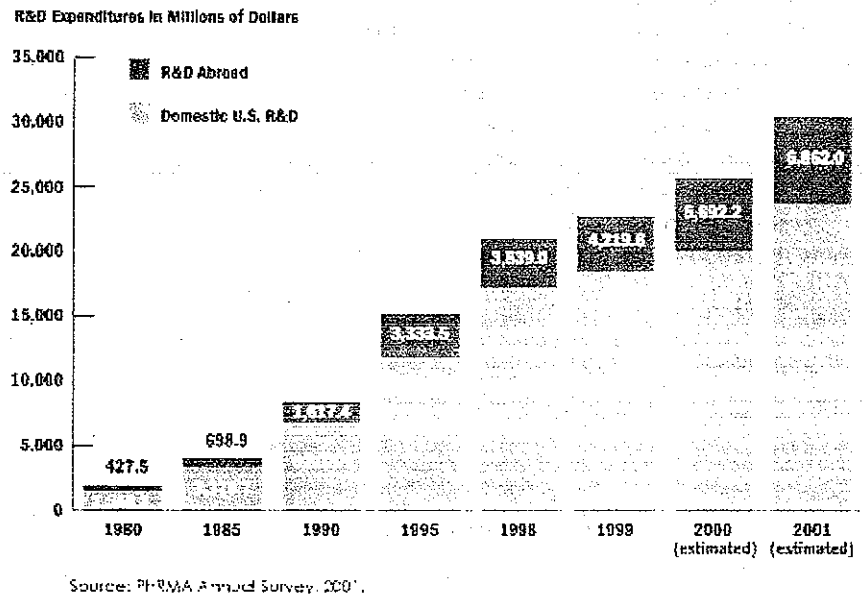
DRUG DEVELOPMENT IN THE PHARMACEUTICALS INDUSTRY

Pharmaceutical Industry Profile 2001
Pharmaceutical Researchers and Manufacturers of America, www.phrma.org

RESEARCH AND DEVELOPMENT INVESTMENT

- In 2001, R&D investment, worldwide, reached $30.5 billion
- 18.7% increase in expenditures from 2000, and triple the R&D expenditure in 1990

Figure 2-1
R&D U.S. AND ABROAD EXPENDITURES, ETHICAL PHARMACEUTICALS, RESEARCH-BASED PHARMACEUTICAL COMPANIES, 1980–2001



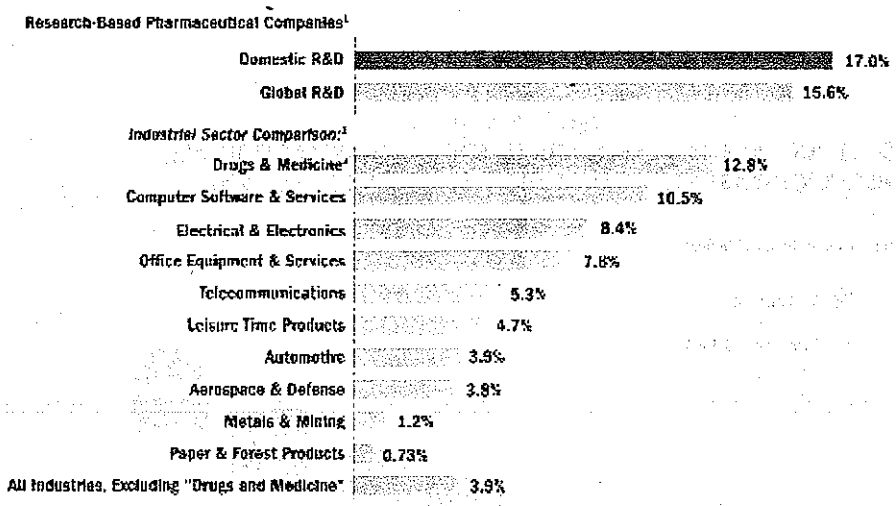
Source: PHRMA Annual Survey, 2001.

Source: Pharmaceutical Industry Profile 2001, Chapter 2, Research and Development – The Key to Innovation, page 12; www.phrma.org

RELATIONSHIP OF R&D TO SALES

- Greater than three times level of R&D investment in drugs and medicine

Figure 2-3
R&D AS A PERCENT OF SALES, RESEARCH-BASED PHARMACEUTICAL COMPANIES AND U.S. INDUSTRIAL SECTORS, 2000



1 "Researched-Based Pharmaceutical Companies" based on ethical pharmaceuticals sales and ethical pharmaceuticals R&D only as tabulated by PhRMA.

2 "Standard and Poor's Compustat - 4 digit SIC codes.

3 "Drugs and Medicine" category based on total R&D and sales for companies classified within the "Drugs and Medicine" sector as tabulated by Standard & Poor's Compustat, a division of McGraw-Hill (includes research- and non-research-based companies).

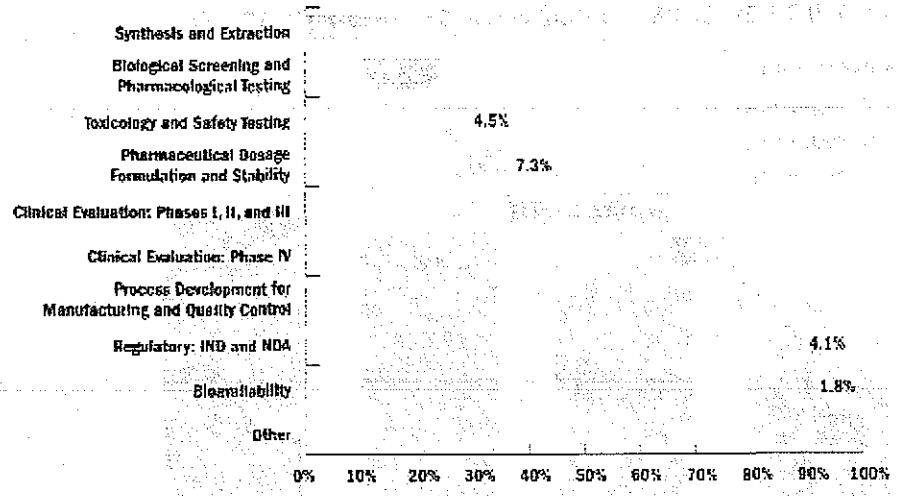
Source: PhRMA, 2001, based on data from PhRMA Annual Survey and Standard & Poor's Compustat, a division of McGraw-Hill.

Source: Pharmaceutical Industry Profile 2001, Chapter 2, Research and Development – The Key to Innovation, pages 13, 15; www.phrma.org

WHERE THE FUNDING GOES

- 36% spent on preclinical studies
- 29.1% spent on Phase I, II and III studies
- 11.7% spent on Phase IV studies, post approval by the FDA

Figure 2-4
ALLOCATION OF DOMESTIC U.S. R&D BY FUNCTION, 1999



Note: Totals may not add exactly due to rounding. R&D functions are not exactly sequential in practice.
Source: PhRMA, Annual Survey 2001.

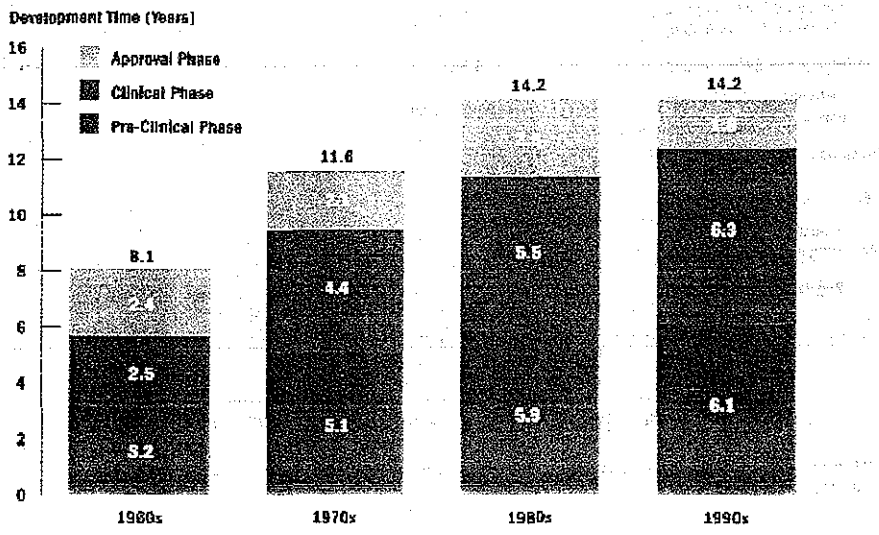
Source: Pharmaceutical Industry Profile 2001, Chapter 2, Research and Development – The Key to Innovation, page 14; www.phrma.org

OTHER ISSUES BEARING ON COST:

TIMELINE FOR R&D

- The Developmental Timeline has increased
  - 8 years to approval in the 1960's
  - 14.2 years to approval in the 1990's

Figure 2-8
TOTAL DRUG DEVELOPMENT TIME FROM SYNTHESIS TO APPROVAL



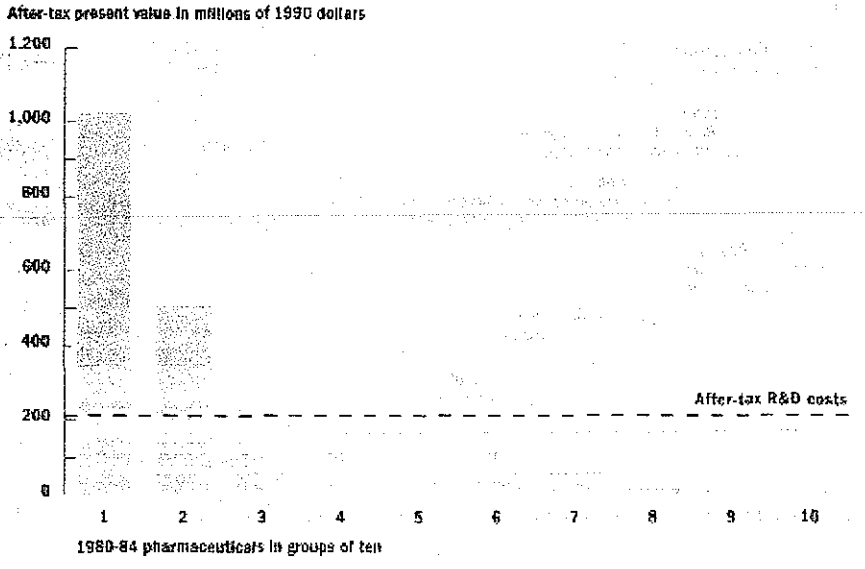
Source: DiMasi J.A., "New Drug Development in U.S. 1963-1999," Clinical Pharmacology & Therapeutics 2001; May; 69(5).

Source: Pharmaceutical Industry Profile 2001, Chapter 2, Research and Development – The Key to Innovation, pages 17, 19; www.phrma.org

SUCCESS FACTOR FOR DRUG CANDIDATES AND FUNDING OF DEVELOPMENT EFFORTS

- Only three out of ten new drug products or new drug entities (introduced 1980-1984) had returns higher than average after tax R&D costs
- Duke University study also showed that the revenues of 20% of the products provided 70% of the returns
- Companies rely on the success of a few products to support their product development pipeline

Figure 2-9
ONLY THREE OF TEN MARKETED DRUGS PRODUCE REVENUES THAT MATCH OR EXCEED AVERAGE R&D COSTS



Note: The drug development costs cited in this chart is after-tax in 1990 dollars for drugs introduced 1980-1984. Based on a separate analysis by The Boston Consulting Group, the pre-tax R&D cost for drugs introduced in 1990 is $500 million.

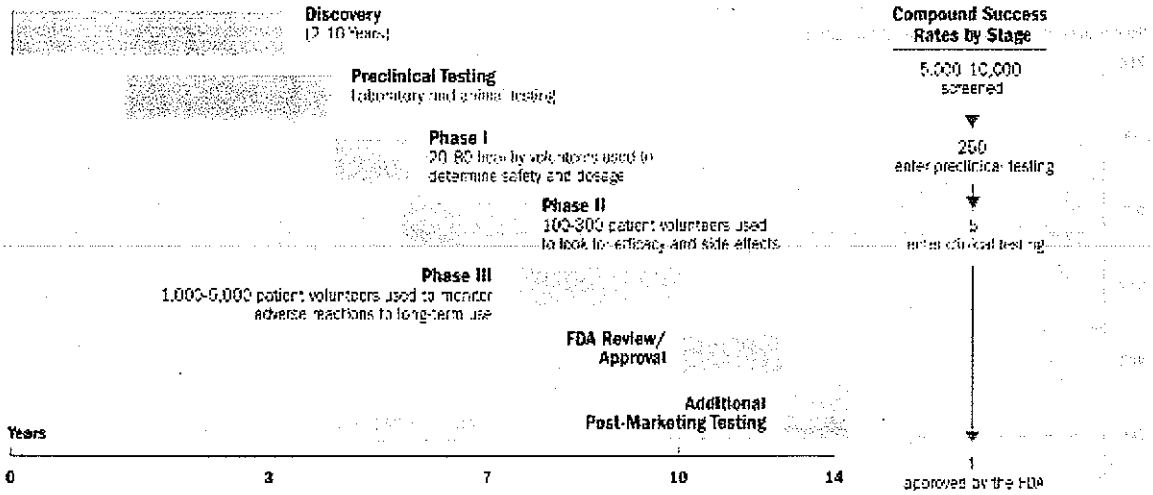
Source: Grabowski, H., and Vernon, J., "Returns to R&D on New Drug Introductions in the 1980s," Journal of Health Economics, Vol. 13, 1994.

Source: Pharmaceutical Industry Profile 2001, Chapter 2, Research and Development – The Key to Innovation, pages 18, 20; www.phrma.org

LIKELIHOOD OF SUCCESS IN DEVELOPMENT

- One in up to 10,000 compounds ultimately becomes a marketed drug
- Rigorous science at the early stages of development is critical to improving the odds of success

Figure 3-1
COMPOUND SUCCESS RATES BY STAGES



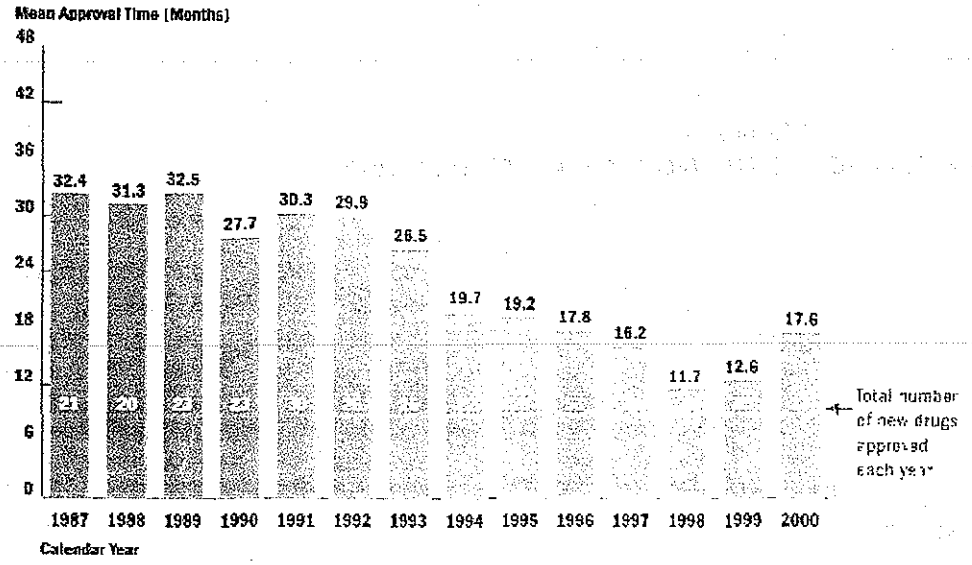
Source: PhRMA, based on data from Center for the Study of Drug Development, Tufts University, 1995.

Source: Pharmaceutical Industry Profile 2001, Chapter 3, Regulatory and Legal Aspects of Drug Development, page 24; www.phrma.org

FDA REVIEW PROCESS – TIMELINE

- FDA review period reduced by almost half since 1987 due to increased pre-clinical efforts and clinical trials supporting more comprehensive regulatory filings, and FDA efficiency
- Safety is a paramount concern throughout

Figure 3-2
MEAN APPROVAL TIMES FOR NEW DRUGS, 1987–2000



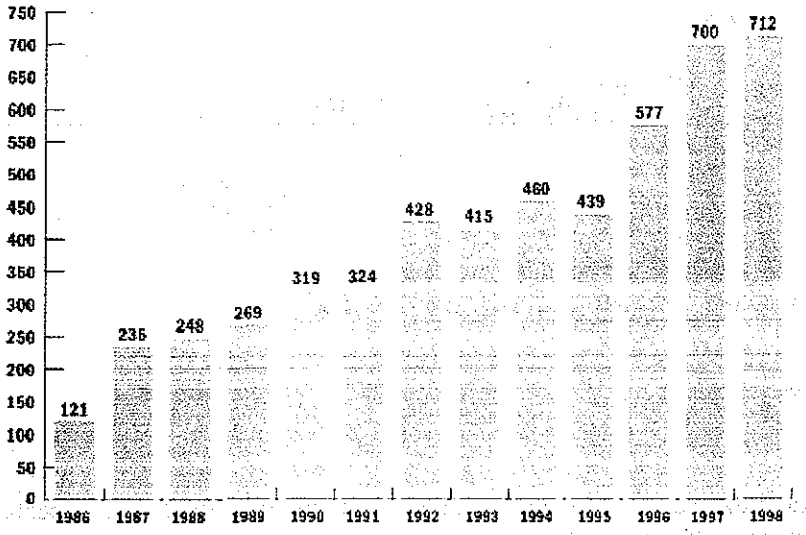
Source: U.S. Food and Drug Administration, 2001

Source: Pharmaceutical Industry Profile 2001, Chapter 3, Regulatory and Legal Aspects of Drug Development, page 25; www.phrma.org

OPTIONS FOR MEETING THE FINANCIAL CHALLENGE

- Opportunities of success optimized through collaboration
  - Development expertise
  - Regulatory support, national and international
  - Marketing expertise, national and international
  - Capital
- The impetus to form strategic alliances has built nearly seven fold in the twelve year period from the mid 1980's to the late 1990's
- The frequency of mergers and acquisitions (shown in Figure 5-8) have grown annually, and have included larger transactions

Figure 5-7
INCREASING FREQUENCY OF STRATEGIC ALLIANCES, 1986–1998



Source: Windhover's Pharmaceutical Strategic Alliances 2000.

Source: Pharmaceutical Industry Profile 2001, Chapter 5, pages 62-63; www.phrma.org

Figure 5-8
MERGERS AND ACQUISITIONS IN THE PHARMACEUTICAL INDUSTRY

2000	G.D. Searle and Pharmacia & Upjohn › Pharmacia Corporation
2000	Warner-Lambert and Pfizer Inc. › Pfizer Inc.
2000	Rhone-Poulenc and Hoechst Marion Roussel › Aventis AG
2000	SmithKline Beecham and Glaxo Wellcome › GlaxoSmithKline
2000	Centecor and Johnson & Johnson › Centecor acquired
2000	Knoll Pharmaceuticals acquired by Abbott Laboratories
2000	Alza Corporation anticipated to be acquired by Johnson & Johnson (subject to Board approval)
2000	The Liposome Company acquired by Elan Pharmaceuticals
2000	Pasteur Merieux Connaught › Aventis Pasteur
2000	Pathogenesis Corporation acquired by Chiron Corporation (non-member)
1999	Monsanto and Pharmacia & Upjohn
1999	AHP/Warner-Lambert and Pfizer/Warner Lambert (pending)
1999	Roche and Genentech
1999	Warner-Lambert and Agouron
1998	Hoechst AG and Rhone-Poulenc Rorer
1998	Sanofi SI and Synthelabo
1998	Zeneca and Astra
1997	Hoffmann-La Roche and Boehringer Mannheim
1997	Nycomed and Amersham
1996	CibaGeigy and Sandoz
1996	Elan and Athena Neurosciences
1995	Knoll and Boots
1995	Glaxo and Burroughs Wellcome
1995	Gynopharma and Ortho-McNeil
1995	Hoechst-Roussel and Marion Merrell Dow
1995	Pharmacia and Upjohn
1995	Rhone-Poulenc Rorer and Fisons
1995	Schwarz Pharma and Reed & Carnrick
1994	American Home and American Cyanamid
1994	Hoffmann-La Roche and Syntex
1994	Pharmacia and Erbamont
1994	Sanofi and Sterling (prescription drug operation)
1994	SmithKline Beecham and Sterling (over-the-counter pharmaceutical unit)
1991	SmithKline and Beecham
1990	Boots and Flint
1990	Pharmacia and Kabi
1990	Rhone-Poulenc and Rorer
1989	American Home and A.H. Robins
1989	Bristol-Myers and Squibb
1989	Dow and Marion
1988	Kodak and Sterling
1986	Schering-Plough and Key
1985	Monsanto and Searle
1985	Rorer and USV/Armour

Source: Windhover's Health Care Strategist, 2000.

II. FORMS OF COLLABORATION

THE RELATIONSHIP BEGINS...

- ♦♦ **INTENTIONS AND OBJECTIVES ARE PARAMOUNT**
- ♦♦ **ENSURE THE AGREEMENT MATCHES THE INTENTIONS OF BOTH SIDES – ASK QUESTIONS!**

- CONFIDENTIAL DISCLOSURE AGREEMENTS
  - Purpose: To exchange Proprietary information under obligations of confidentiality
  - Limited term (often five years)
  - Use of the exchanged information only for the purposes of evaluating the contemplated collaboration
  - "Industry standard" format and terms

- MATERIALS TRANSFER AGREEMENTS
  - Purpose: To exchange of materials to conduct specified experimentation
  - Use limited to specified uses
  - Typically requires exchange of resulting data
  - May include a provision permitting publication of results, subject to confidentiality provisions
  - Materials cannot be transferred to third parties, and any unused materials must be returned or destroyed
  - "Industry standard" format and terms

- CONSULTING AGREEMENTS
  - Purpose: To engage a collaborator, often an individual, in the provision of services of mutual interest
  - Term can be one or multiple years, depending on the objectives for the services
  - Should clearly define:
    - The services to be provided by the consultant
    - The time commitment required
    - Payment terms
    - Ownership and use of the consultancy results, and any inventions
  - Typically includes confidentiality provisions
  - Can be used as an adjunct to other forms of agreement, such as licenses or sponsored research agreements
  - If an academic collaborator, be aware of institutional restrictions on scope, time commitment, and rights in intellectual property
  - If the consultant is an employee of an institution, seek institutional approval and sign off

MORE COMPREHENSIVE FORMS OF AGREEMENT:

- SPONSORED RESEARCH AGREEMENTS
  - Performed under a Research Protocol and Budget
  - Provides for exchange of results obtained
  - Typically includes provisions of confidentiality, and rights to intellectual property developed
  - Often includes publication provisions, if an academic collaborator, subject to obligations of confidentiality
  - Be sure to include a scientific contact within the company to work with the research collaborator
  - Can be developed concurrent with a license or other strategic agreement

AGREEMENTS WITH INCREASING STRATEGIC IMPORTANCE:

- LICENSE AGREEMENTS
- COLLABORATION AGREEMENTS
  - Marketing, manufacture, product development, delivery and formulation
- JOINT VENTURE AGREEMENTS
  - Focus on a field defined by product or service
- MERGERS AND ACQUISITIONS
  - Can involve companies of greater/lesser or approximately same size
  - Asset Acquisitions
  - Formation of a new business entity
  - Spin-outs of some or all technology

III. DEVELOPING THE PROCESS

A SUCCESSFUL COLLABORATION CANNOT BE BUILT WITHOUT:

- ♦♦ **DETERMINING THE INTENTIONS OF THE PARTIES IN WORKING TOGETHER, AND**

- ♦♦ **CLEARLY DEFINING THEIR OBJECTIVES**

CONSIDER:

- **Relationship defined by Industry**
  - Synergistic technologies
  - Service provider becoming collaborator
  - Advantage of broader collaboration to provide guidance for relationship in the future (such as Master Agreements)
  - Customer/Supplier

- **Relationship defined by Technology**
  - Value of Intellectual Property held, and improvements
  - Anticipated future development of the technology field
  - What other technologies will offer alternatives
  - Is the value in Patents, or driven by trade secrets, copyrights or trademarks

- **Relationship between the Parties**
  - On-going participation of seller
  - Allocation of responsibilities, such as R&D and manufacture, marketing
  - Is the collaboration an entry into a broader future collaboration/acquisition
  - Is "relationship building" a purpose for the collaboration
  - Alliance Management

ASK:

What does the client want at the end of the day?

What is important to the deal, and what is not?

What makes a good deal a great deal (and when does it go in the other direction)?

CLIENT AND COUNSELOR SHOULD UNDERSTAND:

How is the collaboration going to move forward, after execution?

What is the effect of not thinking through all aspects of the collaboration?

- **Lengthy and difficult negotiations**
- **Poor future relationships in the future**
- **Project abandoned**

IV. CONTRACTUAL CONSIDERATIONS

The agreement must clearly reflect the obligations and rights of the parties and what is important to each

- Cost
  - Research funding
  - Services funding
  - Option fees for improvements
  - Patent expenses
  - Royalties on earned sales
  - Minimum annual royalties
  - Milestones
  - Patent enforcement expenses
  - Options for fully paid up rights

- Grant clause
  - Exclusive or non-exclusive
  - When can one shift to another
  - Buy-ups or Buy-downs

- Term and Termination
    - Term and patents, pending applications, and trade secrets
    - Termination
        - Unwind provisions
            - Financial considerations
            - Disposition of results
            - Disposition of intellectual property (solely or jointly owned)
            - On-going obligations (such as confidentiality, participation in Intellectual Property Litigation)
        - Termination for cause
        - Termination for convenience

- Due Diligence
    - Development and Milestone Timelines
    - What happens if technical events interrupt the timeline

- Confidentiality and Publications
    - Publications not often issue with companies, but a key issue for academic collaborators
    - Period allowed for removal of the disclosing party's confidential information and patent application filings

- Definitions
    - Test the definitions with a "lay person" reading of the agreement
    - Layering

DRAFTING THOUGHTS

- **DON'T WRITE AN AGREEMENT YOU WOULDN'T SIGN**

- **IF THE AGREEMENT REQUIRES A LAWYER TO UNDERSTAND IT ...**

V. ADDITIONAL THOUGHTS

- **Reevaluate the collaboration positioning through the negotiation process**
  - Have the goals or the objectives of the parties changed?
  - As discussions proceed, are there new opportunities for tailoring the collaboration (broadening or narrowing)?
  - Have outside events changed the needs/wants of the parties?
  - Have internal events changed what parties want/need or can afford?

- **Coordinate stacking provisions for royalties**

- **Consider tax implications**
  - **Joint ventures, spin-outs, wind-ups**
  - **International collaborations**
    - **Manufacture on one shore, fill-finish on another**
    - **Customs duties and COGS**

- **The real cost to the collaborator**
  - **In management time**
  - **In consumption of R&D resources**
  - **In consumption of manufacture resources**
  - **In $$ outlay**

WORK TOWARD A WIN-WIN COLLABORATION

.....

GOOD RELATIONSHIPS ONLY GET BETTER