# Appendix A
# Method of Study

This assessment grew out of the continuing political debate over rising pharmaceutical prices in the United States. The House Committee on Energy and Commerce and its Subcommittee on Health and Environment requested in 1988 that the Office of Technology Assessment (OTA) provide an independent estimate of the "average" cost of bringing a new drug to market, in response to industry claims that the estimated cost of bringing a new drug to market was $125 million. The request was later endorsed by the Subcommittee on Antitrust and Monopolies of the Senate Committee on the Judiciary.

In preparing for a project proposal to OTA's Technology Assessment Board, OTA management concluded that focusing on research and development (R&D) costs alone would be too narrow and that these costs should be studied in the context of the financial returns that investors receive from pharmaceutical R&D. OTA also concluded that the study should examine how Federal policies affect both the costs of and returns on R&D. OTA submitted a proposal to the Technology Assessment Board in June 1989, which the Board approved for initiation in September 1989. (The project was not fully staffed until January 1990.)

The project had four components:

- Analysis of the cost of discovering and developing a new drug;
- Analysis of the financial returns on drug discovery and development;
- Analysis of financial returns in the research-intensive ethical pharmaceutical industry as a whole; and
- Review of the effect of external factors on costs and returns on pharmaceutical R&D, including new drug regulation, tax policy, product liability law, direct R&D subsidies by the National Institutes of Health (NIH) and other government research bodies, and reimbursement policies (both private and public) for prescription drugs.

## Advisory Panel

Every major OTA assessment is advised by a panel of outside experts and representatives of relevant interest groups. The role of the Advisory Panel is to provide guidance in project planning and review of OTA's findings. The panel is not responsible for the final contents of an OTA assessment. OTA chose a 16-member Advisory panel comprising industrial pharmaceutical R&D managers, pharmaceutical industry executives, consumer advocates, physicians, accountants, economists and lawyers. Frederick M. Scherer, Professor of Economics at the John F. Kennedy School of Government at Harvard University served as panel chair. The Panel convened twice during the project, once early in 1990 to give advice about research priorities and directions for the project, and again in May 1991 to review a preliminary draft of the study. Six members of the Panel also participated in a workshop (discussed below), and the Panel was involved in every round of project review throughout the course of the study.

## Site Visits

Early in the project, OTA visited eight pharmaceutical companies (listed in table A-1) to interview senior-level corporate and R&D managers about the R&D process and the economics of pharmaceutical R&D. These interviews were extremely useful in providing a qualitative appreciation for the complexity and cost of pharmaceutical R&D as well as an understanding of how companies track their R&D costs in internal management cost accounting systems. The meetings were not intended to, nor did they, produce actual cost data on new drug development.

## Workshop on the Economics of Pharmaceutical R&D

To explore relevant economic methods and data, OTA engaged in intramural research and also contracted for several papers that were presented at a workshop held in September 1990 at the University of

**Table A-I-Sites and Dates of OTA Visits to Selected Pharmaceutical Companies**

| | |
|---|---|
| Cetus Corporation<br>Emeryville, CA<br>July 19, 1990 | Schering-Plough Corporation<br>Madison, NJ<br>February 12, 1990 |
| Genentech, Inc.<br>San Francisco, CA<br>July 18, 1990 | SmithKline Beecham Corporation<br>Philadelphia, PA<br>June 15, 1990 |
| Eli Lilly and Company<br>Indianapolis, IN<br>April 17 and 18, 1990 | Syntex Corporation<br>Palo Alto, CA<br>July 17, 1990 |
| Merck & Company<br>Rahway, NJ<br>June 19 and 20, 1990 | The Upjohn Company<br>Kalamazoo, MI<br>April 19, 1990 |

California, Santa Barbara. Workshop participants included paper authors, six members of the Advisory Panel with economic or financial expertise, and a small number of outside experts who reviewed and critiqued the papers for revision. (See table A-2 for a list of workshop attendees.) This review greatly enhanced the quality and clarity of the contract papers, some of which became essential pieces of the R&D assessment.

## Review and Revision of Profitability Study

One contract paper, a comparative study of profitability of firms in the pharmaceutical industry with firms in other industries, utilized new methods for analyzing publicly available accounting data to infer economic profits. This study generated a great deal of discussion and critique at the workshop. Because of the potential policy importance of the subject matter and the technical nature of the methods and critiques, OTA initiated a thorough process of revision and review in collaboration with the contractors, William Baber (George Washington University) and Sok Hyon Kang (Carnegie Mellon University).

Baber and Kang submitted a second draft of their contract report to OTA in January 1991, based on the criticisms raised at the 'workshop. OTA contracted with two of the country's foremost experts on profit measurement, Franklin Fisher (Massachusetts Institute of Technology) and Gerald Salamon (Indiana University), as well as the panel chairman, to provide a thorough review and critique of the second draft. These two reviews formed the basis for a third revised draft of the profit study in March 1991, which was then submitted for further review not only to the Advisory Panel but also to Professors Fisher and Salamon and a small number of outside economists who specialize in the pharmaceutical industry.

One outside economist who specializes in the pharmaceutical industry submitted a detailed critique of the third draft of the profit study in July 1991. OTA asked Baber and Kang to reply to the critique. The entire file of comments and replies was then sent back to the two contract reviewers and the panel chair for a final review. These reviews convinced OTA that the methods employed by Baber and Kang to measure profitability in the industry are sound and represent an important advance over previous methods. OTA compiled the entire history of review for the profit study into a single document that is available upon request to interested parties.

## Other Research Activities

In addition to contracting for research on the pharmaceutical R&D process, OTA sought out other sources of data bearing on costs of R&D and returns to the industry from these activities. Data availability was a major problem, particularly data on domestic and worldwide sales of new drugs introduced to the U.S. market during specific time intervals. OTA was able to purchase limited data on domestic sales from IMS America, Inc., a market research firm specializing in surveys of pharmaceutical purchases and prescriptions, but was required to rely mainly on a sales data analysis conducted for other purposes by the Food and Drug Administration. OTA was also able to contract with Stephen Schondelmeyer of Purdue University to provide a report on pharmaceutical sales for drugs that have recently lost patent protection based on IMS America data.

OTA was never able to gain access to IMS data on worldwide sales. IMS International, Inc., quoted OTA a price of over $100,000 for specific data on the ratio of worldwide sales to domestic sales for drugs introduced to the market between 1981 and 1983. OTA used what data were available from existing literature and the sources available to us to conduct an independent analysis of returns on R&D.

OTA was assisted throughout the course of the study by contract papers on specific research issues and topics. Table A-3 contains a list of the major contract papers prepared under the assessment. Papers marked with an asterisk were presented and reviewed at the September 1990 Santa Barbara workshop. Other contract reports were reviewed as appropriate by outside experts and panel members.

**Table A-2—Participants in the OTA Workshop on the Economics of Pharmaceutical R&D, Santa Barbara, California, September 1990**

**Robert B. Helms, Workshop *Chair***
**Resident Scholar**
**American Enterprise Institute**
**Washington, DC**

**Rosanne Altshuler**[a]
**Assistant Professor of Economics**
**Rutgers University**
**New Brunswick, NJ**

**William R. Baber**[b]
**Associate Professor**
**George Washington University**
**Washington, DC**

**William S. Comanor**
**Professor Economics**
**University of California**
**Santa Barbara CA**

**Paul Coppinger**
**Deputy Associate Commissioner for Planning and Evaluation**
**Food and Drug Administration**
**Rockville, MD**

**Richard Frank**
**Associate Professor of Health Policy and Management**
**Johns Hopkins University**
**Baltimore, MD**

**Ronald W. Hansen**
**Associate Dean for Academic Affairs**
**University of Rochester**
**Rochester, NY**

**Sok-Hyon Kang**
**Assistant Professor of Industrial Administration**
**Carnegie Mellon University**
**Pittsburgh, PA**

**Judy C. Lewent**
**Chief Financial Officer**
**Merck & Co. Inc.**
**Whitehouse Station, NJ**

**Albert Link**
**Professor of Economics**
**University of North Carolina**
**Greensboro, NC**

**Alison Masson Keith**[c]
**Assistant Director for Economic Analysis**
**Pfizer, Inc.**
**New York, NY 10017**

**David Salkever**
**Professor of Economics**
**Johns Hopkins University**
**Baltimore, MD**

**Frederick M. Scherer**
**Professor of Economics**
**Harvard University**
**Cambridge, MA**

**Stuart O. Schweitzer**
**Professor and Chair, Department of Health Services**
**University of California**
**Los Angeles, CA**

**Jacob Stucki**
**Vice President for Pharmaceutical Research (retired)**
**The Upjohn Company**
**Kalamazoo, MI 49008**

**Lakshmi Shyam-Sunder**
**Assistant Professor of Business Administration**
**Dartmouth College**
**Hanover, NH**

**Shyam Sunder**
**Professor of Accounting**
**Carnegie-Mellon University**
**Pittsburgh, PA**

**Steven N. Wiggins**
**Texas A & M University**
**College Station, TX**

a Dr. Altshuler was with Columbia University at the time of the workshop.
b Dr. Baber was with Georgetown University at the time of the workshop.
C Dr. Keith was with the Federal Trade Commission at the time of the workshop.

**Table A-3-Major Contract Papers Prepared for the Pharmaceutical R&D: Costs, Risks and Rewards Project**

- **Roseanne Altshuler, Ph. D., Rutgers University, New Brunswick, New Jersey and Henri Chaoul, Ph. D., Columbia University, New York, New York.** *The Effect of Tax Policy on Returns to R&D in the Pharmaceutical Industry: A Methodological Review,* **November 1990.**
- **William R. Baber, Ph. D., C.P.A., George Washington University, Washington, DC and Sok-Hyon Kang, Ph. D., Carnegie-Mellon University, Pittsburgh, Pennsylvania.** *Accounting-Based Measure as Estimates of Economic Rates of Return: An Empirical Study of the U.S. Pharmaceutical/ Industry 1976-87,* **March 1991.**

**William R. Baber, Ph. D., C.P.A., George Washington University, Washington, DC, Ronald Ross, Ph. D., and J. Raymond Apple, M. B.A., Georgetown University, Washington, DC.** *Research and Development Accounting Issues With Specific Reference to the U.S. Pharmaceutical Industry,* **December 1990.**

**Lester W. Chadwick, C. P.A., Ph. D., University of Delaware, Newark, Delaware.** *Pharmaceutical/ R&D Study, Accounting for R&D.*

**Robert Mullan Cook-Deegan, M. D., Consultant, Rockville, Maryland,** *Trends in Sciences, Technology, and Drug Discovery,* **(incorporated in edited form as chapter 5 of the final report) October 1991.**

**W. Gary Flamm, Ph. D., F. A.C.T., and Michael Farrow, Ph. D., SRS International, Inc., Washington, DC.** *Recent Trends in the Use and Cost of Animals in the Pharmaceutical Industry,* **April 1991.**

- **Richard G. Frank, Ph. D., and David S. Salkever, Ph.D, Johns Hopkins University, Baltimore, Maryland.** *Pricing, Patent Loss and the Market for Pharmaceuticals,* **December 1990.**

**Alan M. Garber, Ph. D., M. D., Palo Alto Department of Veterans Affairs Medical Center and Stanford University, Pato Alto, California, Ann E. Clarke, M. D., Dana Goldman, B. A., Stanford University, Pato Alto, and Michael E. Gluck, Ph. D., Office of Technology Assessment, U.S. Congress, Washington, DC.** *Federal and Private Roles in the Development and Provision of Alglucerase Therapy for Gaucher Disease, OTA-BP-H-1O4* **(Washington, DC: U.S. Government Printing Office, October 1992).**

- **Elizabeth J. Jensen, Ph. D., Hamilton College, Clinton, New York.** *Rates of Return to Investment in the Pharmaceutical Industry: A Survey,* **September 1990.**

**Albert Link, Ph. D., University of North Carolina, Greensboro, North Carolina.** *Tax Incentives and the U.S. Pharmaceutical Industry,* **November 1990.**

- **Stewart C. Myers, Ph. D., Massachusetts Institute of Technology, Cambridge, Massachusetts and Lakshmi Shyam-Sunder, Ph. D., Dartmouth College, Hanover, New Hampshire.** *Cost of Capita/Estimates for Investment in Pharmaceutical Research and Development,* **January 1991.**

**Stephen W. Schondelmeyer, Pharm.D., Ph. D., University of Minnesota, Minneapolis, Minnesota,** *Economic Impact of Mu/tip/e Source Competition on Originator Products,* **February 1992.**

**Gordon Sick, Ph. D., University of Calgary, Calgary, Alberta, Canada** *Pharmaceutical/ Industry R&D and the Cost of Capita/,* **February 1992.**

**Ellen S. Smith, M. B.A., Woodcliff, New Jersey.** *Third Party Payment for Unapproved Uses of Approved Drugs and for Medical Care Associated With Drug Clinical Trials,* **January 1991.**

**Steven Wiggins, Ph. D., Texas A&M University, college Station, Texas.** *Pharmaceutical R&D Costs and Returns* **December 1989.**

**NOTE: Contract papers marked with an asterisk were presented and reviewed at the September 1990 workshop held in Santa Barbara, CA.**

In addition to other data collection and analysis tasks, OTA conducted a survey of clinical trial sizes for drugs approved in the late 1970s versus the mid-1980s.

## Report Review Process

A preliminary draft of OTA's report was submitted for review and critique to the Advisory Committee in April 1991. The Panel meeting in May 1991 was devoted to a discussion and critique of that draft and suggestions for further research. OTA spent the next year continuing the research process outlined above, searching for data, verifying the accuracy of data, and conducting analyses. Sections of the draft were submitted for special review to selected panel members and outside reviewers throughout the spring of 1992, and revisions were made in the draft before it underwent the general review. (A total of 43 people reviewed targeted sections of the report throughout this period.)

The full second draft of OTA's report was distributed for review to the Advisory Panel and a group of outside experts and interested parties in August 1992. A total of 122 people were sent the second draft, and 63 separate replies were received. OTA reviewed and revised the draft as appropriate in response to these comments,