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Merck: Conflict and Change

We never try to forget that medicine is for the people. It is not for profits. The profits follow, and if we have remembered that, they have never failed to appear.

—George W. Merck

The 2002 fiscal year had just ended, and Ray Gilmartin, Merck's CEO, had been under pressure for some time as Merck's stock market performance had trailed that of competitors' and concerns had surfaced about the strength of Merck's drug pipeline. Recent press articles and books had expressed concern about Merck's ability to respond to recent changes in the environment. They pointed to competitors' successful strategy of acquiring drugs and marketing them aggressively via their significantly larger sales forces, and to the market opportunities that Merck had failed to convert to its own advantage. And, while many analysts acknowledged Merck's historical research prowess, they questioned whether it was enough, especially in light of its imminent patent expirations and perceptions of a thin pipeline.[1]

Yet, Ray Gilmartin was confident of his company's future. Hired to lead Merck in 1994, he could point to significant strategy decisions and organizational changes that had allowed Merck to respond to market shifts without sacrificing its identity as a "science-led" company. Nevertheless, he still wondered whether he had gone far enough. Was Merck adequately oriented to the market and to the changes taking place in the industry? Could it move further in that direction without compromising the company's historical strength in science and focus on breakthrough drugs?

Background

Until the mid-twentieth century, German and Swiss universities and companies dominated pharmaceutical research. Merck, a manufacturer of fine chemicals in Germany, had only a small sales presence in the United States until the First World War. In 1917, the U.S. government seized the stock of all German-held subsidiaries; the Merck family and other investors bought back the company's

[1] See for example, "Out of the Merger Rush, Merck's on a Limb," *The New York Times*, Money & Business Section, August 4, 2002; "Merck Could Use a Few Pep Pills," *Business Week*, December 17, 2001 and "The $10 Billion Pill," *Fortune*, January 20, 2003.

Professor Clark Gilbert and Research Fellow Ratna G. Sarkar prepared this case. HBS cases are developed solely as the basis for class discussion. Cases are not intended to serve as endorsements, sources of primary data, or illustrations of effective or ineffective management.

stock and incorporated as a U.S. firm with no ties to the German parent. Mergers with other small U.S. chemical firms followed, and scale economies, coupled with necessity, led to a large R&D push at Merck. By the start of World War II, Merck Research Labs (MRL) was the leading pharmaceutical research institution in the United States. It had a world-class reputation, attracting top researchers in the fields of chemistry, biology and pharmacology. A string of novel drugs emerged, like streptomycin to treat tuberculosis and penicillin to address an array of previously-deadly bacterial infections. Three of the key technologies of the period—vitamins, antibiotics and hormones—were developed at MRL. These solidified Merck's reputation and boosted its profitability to the top-most levels in the industry.

In the 1970s, biochemistry and the study of enzymes revolutionized pharmaceutical research. Merck recruited Dr. Roy Vagelos, an MD from Columbia University and a distinguished enzyme chemist. He was appointed head of MRL in 1976, and he led the labs into very successful cutting-edge molecular research. During this period, Merck opened up entirely new therapeutic areas and enhanced its reputation for bringing breakthrough drugs to the market, many of which became "blockbusters."[2] Merck held leading positions in several therapeutic areas.[3] During the 1980s, sales more than doubled, profits tripled, and from 1987 to 1990, each year, the company was among the top 10 most valuable companies ranked by *Business Week.*[4] Many competitors sought to emulate Merck's research-driven business model. Merck's profitability was among the highest in the industry and investors were rewarded for their investment in the "science-led" company (see **Exhibits 1a** and **1b**).

The Drug Development Process

The modern drug development process is dependent on nascent screening technologies and complex scientific and statistical tools to identify disease targets in the human body and potential drug candidates to treat them. This complex discovery process, coupled with a demanding regulatory environment, results in an average drug development time of over 15 years and an average R&D expenditure of over $800 million[5] (see **Exhibit 2**). The process begins with a pre-clinical discovery phase as researchers attempt to isolate a biological target for intervention, to identify a stable agent that will safely suppress the disease, and to find a reliable indicator of the efficacy of the agent. Then, the agent's efficacy is validated in animal trials and the company files an Investigational New Drug application with the Food and Drug Administration (FDA).

Once it enters the FDA's regulatory system, a drug's safety and efficacy must be established in human clinical trials through a three-phase process. During Phase I, the drug is given to a small number of healthy volunteers to assess its safety and activity at different dosage levels. During Phase II, the drug is studied for longer durations in patients suffering from the disease to provide

[2] In the mid-1980s and 1990s, a blockbuster drug was one whose annual sales had reached over $500 million. By the early-2000s, a blockbuster was one whose annual sales had reached at least $1 billion.

[3] For example, in 1987, Merck introduced the top-seller *Mevacor*, a novel treatment for artherosclerosis or high cholesterol, followed by *Zocor* in 1992 which became a blockbuster. Also, in the mid-1980s, Merck's blockbuster drug *Vasotec* provided a novel treatment of hypertension or high-blood pressure, followed by *Cozaar* in 1995, another blockbuster which kept Merck in the forefront of the hypertension arena. By 2001, Merck would own the leading or second most popular drug in five therapeutic areas: *Zocor* for artherosclerosis, *Cozaar* for hypertension, *Fosamax* for osteoporosis, *Vioxx* for arthritis and *Singulair* for asthma; together they would account for over 70% of Merck's 2001 human pharmaceutical revenues. Most of these drugs were developed at Merck or licensed from partners under Dr. Vagelos who was CEO from 1985 to 1994.

[4] See "The Business Week Top 1000: America's Most Valuable Companies," Business Week, April 17, 1987, April 15, 1988, April 14, 1989 and April 13, 1990.

[5] This figure, developed in a November 2001 report from the Tufts Center for the Study of Drug Development (http://csdd.tufts.edu) includes the cost of capital and expected cost of failures at each step in the process.

preliminary evidence of safety and efficacy and to establish the appropriate dose for larger studies. In Phase III, randomized, double-blind tests with placebo control[6] are performed on larger groups of patients to gather the additional safety and efficacy information that is needed to evaluate the overall risk/benefit of the drug and to provide an adequate basis for labeling. At the end of Phase III, the manufacturer submits a New Drug Application for review by the FDA. The application, sometimes exceeding 100,000 pages in length, compiles the research completed during the pre-clinical research and the three clinical trial phases, and includes full details of the drug's formula, production, labeling, and intended use.

Over its life-cycle, a drug's target patient population and its reach is largely determined by its FDA-approved label which discusses chemical composition, indications, contra-indications, side-effects, safety issues and dosages. The label can only contain medical efficacy claims that have been established via rigorous clinical tests on an appropriately-sized and designed patient population, and have been approved by the FDA. The initial drug label takes shape during the pre-clinical and clinical phases of its development, driven by medical and marketing needs and limited by what can be scientifically established. The aim is to send the most scientifically and competitively compelling claims to the FDA for inclusion on the drug label.

Often, various tests and trials are designed and initiated not for inclusion on the initial drug label, but as follow-up studies whose results may be available after the drug has been launched. Subject to FDA approval, these changes to the drug label may be timed to appear at specific stages in a product's life-cycle to address competitive and regulatory issues. After the launch of a drug, new studies may also be conceived to expand a drug's medical benefit claims. All such clinical research, whose FDA-approved claims will have a post-launch effect on drug labels, is known as Phase V research at Merck.[7] These clinical studies are often "outcome studies"—studies that focus on the drug's effect on quality of life and mortality and morbidity in large populations. These post-marketing clinical studies can greatly influence the adoption and long-term success of the drug.

Industry and Economics

The pharmaceutical business is characterized by high fixed R&D costs incurred over a period of many years for distant and risky returns. It is estimated that, on average, for every 5,000 molecules discovered, only a couple of hundred are worth investigating, only one ever reaches the market, and fewer than a third of marketed drugs actually achieve enough commercial success to recoup their R&D investment. However, when a new drug is a breakthrough therapy for a large-population disease, it can command a premium price under patent protection and become a blockbuster drug that contributes to the industry's overall hefty profit margins.

In the 1990s, operating profit margins as high as 40% were common among leading drug makers. By 2001, price competition and buyer demands exerted pressure on margins, but the return on human pharmaceuticals sales still exceeded 30% (see **Exhibit 3**), more than double that of the average corporation in the S&P 500 Composite Stock Index. An S&P industry survey[8] reported that during

[6] In a randomized, double-blind, placebo-controlled test, one group of patients is given the drug while another group receives an inert substance. Neither the patients nor their doctors know which patients are actually receiving the drug being tested.

[7] At other pharmaceutical companies and in the business press, these studies may be called "Phase IV" studies. Merck calls studies "Phase IV" if they are required by agencies like FDA as part of the registration approval. They call studies "Phase V" if they are new indications for approved products or studies desired by marketing to provide new information for an approved product.

[8] See the December 2002 Healthcare: Pharmaceuticals survey at www.netadvantage.standardpoor.com.

1997–2001, drug-makers' net earnings as a percentage of sales averaged 15.7%, compared with about 5.7% for general industry. The industry's average return on equity remained above 25%, among the highest of all industries.

A "Science-Led" Company

Since its earliest days as an independent pharmaceutical company, Merck had steadily built up its reputation as a research powerhouse. MRL was led by top scientists with a core strategy to develop breakthrough drugs in new therapeutic categories. MRL's success was also manifested in its leadership in patent filings which, by the 1990s, led even those of its strongest competitors (see **Exhibits 4a** and **4b**).

In 1985, MRL-head Vagelos was appointed CEO, and Dr. Edward Scolnick was made head of MRL.[9] Scolnick followed the direction set by Vagelos, continuing to raise MRL's profile and access to resources, attracting the best scientific talent to Merck and encouraging them to pursue their research interests and to publish their work in the top scientific journals. For many PhDs and post-docs at leading universities, the only non-academic job they would even consider, and which their advisors would permit, would be at MRL. A top molecular biologist described why he made the switch from academics to Merck: "I had known about Merck and Ed Scolnick even when I was at MIT. It was well known that at Merck, scientists are valued, work is published, and first-rate science is done. Among chemists, Merck is a dream job, its reputation is unbelievable, and it is successful at hiring the best right out of graduate school. Tischler, Vagelos, Scolnick—that's a gigantic scientific legacy. "

In the very complex endeavor of discovering new disease pathways and new drugs, MRL had especially honed its skill in a few areas. It was known to set extremely high standards in assessing projects in the pre-clinical phases and in Phase I. Each molecule had to meet very high internal standards of efficacy and safety before Phase II work began. MRL's propensity to develop extremely detailed biological and chemical drug profiles had also helped Merck garner an industry-wide reputation for being trusted and esteemed at the FDA, whose approval rates for Merck drugs—estimated by outside scientists at about 70%—had historically been higher than the industry average of 50%. This high success rate, coupled with a reputation for very few drug withdrawals or recalls, had been a source of scientific pride at MRL and also of great economic benefit to Merck.

In the 1980s and early 1990s Roy Vagelos ran Merck with the help of the "Chairman's Staff" (see **Exhibit 5**). The EVP of Human Health sales and marketing[10] was the sole line manager and the single point of market contact. Under that EVP, the marketing function was organized geographically. Country and region managers, who had P&L responsibility, had no direct input at the chairman's table in budgeting and resource allocation decisions. MRL, organized by drug development phases and by scientific disciplines, seemed to be the ultimate arbiter of key strategic decisions. A senior marketing executive recalled, ''In my 30 years of experience here, there is no doubt about who leads this organization. It's the scientists. I'm not saying it's good or bad. The first decisions are made by scientists and veto decisions are made by scientists. There has never been any doubt about whose call it is."

MRL's power was evident in the matter of Phase V or post-marketing clinical studies, i.e., clinical drug research intended to improve the positioning of the drug after it had been introduced in the

[9] Scolnick had earned an MD from the Harvard Medical School in 1965, conducted ground-breaking research in protein synthesis, animal virology and tumor genetics for 17 years at the National Institutes of Health, and had joined Merck in 1982.

[10] The sales and marketing function for pharmaceutical products at Merck is now known as "Human Health."

marketplace. At Merck, three groups were equipped to conduct Phase V studies: Clinical Sciences within MRL, and two clinical development groups, created in the late 1980s within the marketing organizations (one responsible for the studies within the U.S. and the other for studies outside the U.S.). Every clinical study, including every Phase V study or clinical development study, was vetted by the Clinical Research Review Committee (MRL's peer review committee) for safety and efficacy parameters and strict quality control. During the late 1980s and early 1990s, most Phase V studies were conducted by Clinical Sciences within MRL and they were usually follow-up studies about drug safety. The clinical development groups within marketing conducted few clinical studies, and they focused mostly on local marketing needs.

One marketing manager commented, "MRL gave us the drug, it was best in class, and we sold it. Marketing was 'allowed' in much later in the process. It was a good strategy, it worked at the time." While marketing did take a back seat to MRL, the repeated financial success of the company's blockbuster drugs and their contribution to Merck's industry reputation continually reinforced the view that breakthrough drugs come from great science and MRL was at the core of that strategy.

The Changing Environment

In the 1980s and 1990s, major changes occurred in the pharmaceuticals business. The 1984 Hatch-Waxman act made it easier for generics manufacturers to enter the market. This meant that as soon as a drug came off-patent, it could lose half or more of its market share overnight. In the U.S., for drugs that come in countable units such as tablets and capsules, the market share of generic prescription drugs in units sold increased from 19% in 1984 to 43% in the 1996.[11]

New technologies lowered the critical mass needed for effective pharmaceutical R&D. Smaller companies entered the drug discovery and development business, often in collaboration with Merck's competitors. Product exclusivity periods declined sharply as competitive drugs within the same therapeutic category emerged more rapidly than before (see **Exhibit 6**). Referring to the accelerating rate of competitive response, a marketing VP commented, "Then, Merck's drugs were first in class, and we defined and held the markets for certain types of drugs. Today, we have less than 6 months of product exclusivity, a lot of the scientific information is shared (with competitors) and this can result in very minor perceived product differences."

The biggest change came in the early 1990s. Large, powerful managed care organizations (MCOs) began restricting the type, number and prices of drugs on their formularies.[12] As a result, sales and growth in the pharmaceutical industry slowed dramatically, leading to a 35% decline in drug company valuations during the first half of the decade.

The overall effects of these changes in the business of discovering, obtaining regulatory approval and selling drugs can be appreciated in the drug revenue curves (see **Exhibit 7**). In the 1980s, the release of a new drug coincided with a long period of information dissemination to physicians via the sales force and scientific forums. With patent protection and few competitors, sales for a drug would

[11] Since countable units do not include injectable drugs and liquid prescriptions, it is likely that the share of generics is understated. Source: July 1998 Congressional Budget Office Report, "How Increased Competition from Generic Drugs has affected Prices and Returns in the Pharmaceutical Industry."

[12] The two type of MCOs—health maintenance organizations or HMOs and pharmacy benefit managers or PBMs—get paid by employers to help manage employee health-care costs. MCOs maintain "formularies" (lists of approved drugs in each therapeutic category) and demand justification for including expensive, patented drugs rather than cheaper generics. From 5% in 1980, the share of the U.S. population covered by MCOs rose to 80% in 1993, and the share of prescriptions managed by them had risen to 73%.

ramp up steadily over 10 years, plateau as the market began to get saturated, and then decline gradually as new patented drugs or clinically tested cheaper generics began to enter the market. Doctors would encourage long-term patients to continue taking the original drug in the interest of comfort and safety. A decade later, a company had only a short window within which to establish the sales of even a leading drug in a category. During that period, physicians, patients, insurers and MCOs were 'blitzed' with information from competitors offering similar products. Even as a drug category matured, generic offerings would appear, threatening precipitous sales declines.

Within Merck, these external challenges triggered a rethinking of the research-driven business model. Merck Chairman and CEO P. Roy Vagelos launched a program called the "New Reality" which featured company-wide cost cutting measures to address declining margins. In the early 1990's, Vagelos advocated a merger with Pfizer to combine Merck's research success with Pfizer's marketing capability, but Merck senior management preferred organic growth and Pfizer management was not interested in a merger. R&D investment and funding for sales promotion and detailing declined as Merck searched for alternative business models in the new environment. In 1993 Vagelos championed vertical integration into managed care through the acquisition of Medco Containment Services, the largest pharmaceutical benefit manager. During this period, Merck also entered the generic drug business with the aim of providing a full line of products for distribution in the hopes of keeping Merck's innovative drugs on managed care formularies.

Other companies responded to these industry changes with a variety of tactics. Several merged or acquired divisions from others in order to gain advantages in particular therapeutic markets by enlarging their research organizations, enhancing their drug pipelines or increasing their market span.[13] Aiming for a larger share of physician attention, pharmaceutical companies doubled their sales forces between 1995 and 2001 to 80,000 sales reps.[14] They also tried to extend the productive lives of their drugs by applying for patent extensions for minor variations of the drugs.

Until the early 1990s, clinical studies established the safety and efficacy of a drug, and provided the basic information needed by physicians and pharmacists and required by the FDA. As the number of drugs for each medical condition increased, the target audience, which now included MCOs and consumers, began to demand studies on overall outcomes (mortality and morbidity, quality of life), on cost effectiveness relative to competing therapies, and on convenience and patient-compliance to the drug regimen.[15] Drug companies were forced to study increasingly larger groups of patients, over longer periods of time, to establish the medical outcomes that would win them a slight edge in the race. Even after a drug was launched, companies funded huge after-market studies of thousands of patients worldwide, in an attempt to improve its label. A company's willingness to conduct the necessary sophisticated and lengthy trials could make the difference between an excellent label with market leadership and a "me-too" drug. A senior Merck executive emphasized the change: "In the past, the molecule was the product, but now the label is the product."

In the early 1990s the FDA, for the first time, allowed "direct-to-consumer" or DTC advertising of prescription drugs in print, television and other consumer media. By 1999, 50 pharmaceutical companies had spent $1.7 billion, or 10% of all promotion costs, to advertise 81 prescription drugs in 53 therapeutic classes directly to the consumer. Studies showed that of patients who discussed an advertised drug with their doctor, 60% received a prescription for it. Also, aging baby boomers were

[13] For example, from 1990 to 2001, there were 12 mergers worth $1 billion or more that were absorbed into top pharmaceutical companies worldwide; 19 different companies or divisions of companies were involved in those mergers, resulting in six large firms (Johnson & Johnson, Novartis AG, AstraZeneca PLC, Pfizer Inc, GlaxoSmithKline PLC and Hoechst AG).

[14] "Making more of Pharma's Sales Force," *McKinsey Quarterly*, Issue 3, 2002.

[15] These types of studies are classified as Phase V or outcomes studies at Merck.

receptive to the idea of paying for and using "lifestyle-enhancing" drugs to treat conditions like baldness, anxiety, erectile dysfunction, arthritis, memory loss and aging skin. Pfizer, for example, embraced this drug category, and used DTC advertising to create a huge demand for its products. In 1992, its licensed antidepressant *Zoloft*® entered the market and reached annual sales of $2 billion by 1999. In April 1998, it introduced *Viagra*®, for the treatment of erectile dysfunction, and within a year, its annual sales exceeded $1 billion, placing it among the most successful drug launches in history. Pfizer also marketed drugs for Alzheimer's, obesity and insomnia.

Rising Cholesterol: The Zocor Drama at Merck

A high-profile battle in the anti-cholesterol arena typifies some of the challenges Merck faced in responding to industry trends in the 1990s. With its discovery of the statin drug *Mevacor*®, Merck had held a leading position in this therapeutic area since the mid-1980s. In 1988 in Europe, and in 1992 in the U.S., it introduced the advanced statin *Simvastatin* in the form of a new drug called *Zocor*®, whose label clearly established its efficacy in reducing cholesterol. Soon after *Zocor* was launched, a group of Scandinavian doctors approached Merck medical directors in Scandinavia to strongly petition MRL for a Phase V *Zocor* outcomes study on overall mortality and morbidity in patients with coronary heart disease. At the time, large marketing-driven studies of non-safety related outcomes were underemphasized at Merck. A senior marketing manager explained, "The emphasis was on Phase II, Phase III, and then MRL wanted to move on. Phase V research was not attractive, they were not rewarded or promoted for it, the best MRL folks did not want to do it." Per Wold-Olsen, head of marketing in Scandinavia at the time, had to argue very strenuously with MRL before the *Zocor* 4S study (Scandinavian *Simvastatin* Survival Study) was approved, funded and conducted by MRL.[16]

The 4S study was considered a "home run" at Merck. It established that *Zocor* lowered mortality and morbidity in patients with coronary heart disease. Marketing started emphasizing its outcomes effects and long-term safety. One manager estimated that the 4S study alone had boosted sales by at least 50% and many agreed that *Zocor* had been critical to driving Merck's overall sales growth at the time. Additionally, with the 4S study, Merck launched a revolution. Patient awareness of cholesterol-reduction as a major health issue and doctors' embrace of statins as effective and safe treatment for cholesterol caused the market to grow tenfold to an estimated 25 billion dollars.

Unfortunately, despite its scientific leadership in this area, Merck was not able to command the cholesterol market for very long. Pfizer, recognizing a gap in its drug line-up, teamed up with Warner-Lambert in 1996 to co-market the latter's new anti-cholesterol drug *Lipitor*®. *Lipitor* was twice as effective as *Zocor* on a milligram basis so its starting dose could be half that of *Zocor*. *Lipitor* entered the market with clinical results showing that it reduced LDL or 'bad' cholesterol more dramatically than *Zocor*. Additionally, *Lipitor's* label stressed its efficacy in lowering trigylcerides, a factor that physicians said was of importance to them. Although *Zocor* also is effective in lowering triglycerides, Merck's scientists held that triglycerides were not medically relevant and insisted that an elevated triglyceride level was not an independent risk factor. Despite the availability of favorable triglycerides data, marketing's request for its inclusion in the *Zocor* label was not accepted.

Pfizer expanded its sales force from 2,800 to 4,200 reps, aggressively targeted patients through DTC marketing, detailed high-prescribing doctors and cardiac-care opinion leaders, and spent about

[16] The 4S study, a randomized trial of cholesterol reduction in 4,444 coronary heart-disease patients, was published in the *Lancet* in November 1994. It reported that after five years of *Zocor* use, patients reduced their cholesterol by 35%. More importantly, *Zocor* reduced total mortality by 30% and coronary mortality by 42%. Patients on *Zocor* lived longer, had fewer hospital readmits and fewer days in hospital.

50% more on promoting *Lipitor* than Merck did on *Zocor.* Within a year after its introduction, *Lipitor* had a 26% market-share to *Zocor's* 27%, and it had 28% of new prescriptions versus 27% for *Zocor.*[17] When American Home Products showed an inclination to acquire Warner-Lambert, Pfizer stepped in and acquired *Lipitor* and Warner-Lambert for $116 billion in early 2000.[18]

MRL head Ed Scolnick characterized the *Zocor* debacle as, "It's one of the worst things that's happened to us since I've been here. It is still with us today." A senior marketing manager commented:

> *Zocor*, despite its financial contribution, is a terrible case of failure on Merck's part. This experience brought out the inadequacies in marketing, inadequacies in the dialog between research and marketing, and the inadequacy of the Merck view that nothing important happened after the New Drug Application (submitted to the FDA). It forced us to face the fact that each drug entered a dynamic, changing world that we needed to manage and respond to.

But, reacting to these intensifying external trends proved difficult for Merck. The heavy push on sales, life-style drugs and DTC advertising was often viewed with distaste by many within the Merck organization. A senior research scientist at Merck said, "Many other drug companies are successful because they shout louder, not because they make better drugs."

Ray Gilmartin: A Bend in the Road

In June 1994, Ray Gilmartin, CEO of Becton Dickinson, a medical equipment company, was hired to succeed Roy Vagelos as CEO of Merck. An engineer by training and an MBA from Harvard, Gilmartin entered a company strongly organized along functional lines, with research clearly at the center. Ed Scolnick remained as head of MRL.

Shared Values, Structure and Strategy

On his arrival at Merck, Ray Gilmartin observed MRL's dominant role in the organization and in all the company's decision-making processes. He also recognized that many industry analysts were questioning the value of expensive drug research, and instead advocating a strategy of pushing large-volume "me-too" drugs through DTC advertising, and aggressively pursuing patent extensions. Gilmartin saw that at Merck, there was a deep-rooted belief in developing the "best molecule" which would then sell on its own clinical merits, and that the pre-eminence of MRL had often left the marketing function sidelined.

Individual meetings with the top managers in the company convinced Gilmartin that Merck's focus on being a science-led company was deeply ingrained in every aspect of the company. It was the reason so many had chosen to come to Merck, and it had become a part of their self-identity. He started to believe that the trend towards me-too drugs and scientific shortcuts, started under Vagelos, should be rejected. He also heard managers' concerns about productivity losses due to strong functional identities and competitiveness within the organization. In particular, he felt that the historical relationship between research and marketing had become especially limiting in the current

[17] By 2002, *Lipitor* would reach $7.2 billion in annual sales and have a 42% percent market share, while *Zocor* would have 32% of the market.

[18] Pfizer's acquisition of Warner-Lambert resulted in a merger of two of the fastest growing companies in the industry, with a combined annual R&D budget of over $ 4.7 billion, and the biggest sales force of about 8,000 sales reps.

environment. Merck's world-class drugs would not now sell themselves—it would need a world-class marketing and sales organization, almost a new marketing philosophy, to re-capture industry eminence and commercial success. Ways had to be found to elevate the skills, role and prestige of marketing.

At the time, marketing was divided into domestic and international marketing, and each was organized geographically by regions. A single EVP of Human Health had filtered the reports of product and country managers up to Vagelos. Marketing was considered a staff function, supporting the sales function with sales materials and data as needed. A long-time marketing manager described the situation at the time, "In the 1980s and early 1990s, marketing's drumbeat was: we have to be successful in seven strategic markets: France, Germany, Scandinavia, Japan, etc. 'Strategic Plans', produced by each country's marketing group were really 100-page documents full of tactical details like local head count needs; there was little or no strategy in them."

Unlike Vagelos, Gilmartin wanted more line managers to report directly to him. He envisioned a flatter, broader organization with more line responsibility at every level. He eliminated the position EVP of Human Health and replaced it with three marketing presidents who reported directly to him (see **Exhibit 8a**). David Anstice, who had been at Merck since 1974 and had served as a senior vice president of marketing in Europe in Roy Vagelos's organization, was promoted to the direct-report position of President of U.S. Human Health and Canada, making him responsible for marketing and sales of the blockbuster franchises in Merck's largest market. Per Wold-Olsen, who had led the demand for the highly successful 4S study on *Zocor*, and who, under Vagelos, had been head of a small worldwide marketing group, was promoted to the position of President, Human Health, Europe. Each of their marketing organizations now had its own sales force. Henri Lipmanowicz assumed responsibility for the other markets in Asia, Africa and Latin America. These changes put Anstice, Wold-Olsen and Lipmanowicz on Gilmartin's new Management Committee, with more direct access to resources and more direct responsibility for Merck's financial and market performance.

Gilmartin convened an off-site meeting with his new Management Committee to agree on a series of strategic choices. First, the team agreed that the discovery and commercialization of breakthrough drugs was the only viable strategy for responding to the cost containment environment. Then, to implement this strategy, they agreed to accelerate investment in innovative R&D to bring breakthrough products to the market and to reinvest in sales and marketing capability needed to launch the products in late-stage development. Medco would be operated as a stand-alone company, focused on bringing value to its employer and managed care customers. Finally, the team agreed that Merck would not consider large-scale mergers which might provide short term benefits, but would not add to long term growth prospects of the company.

Getting Drugs to Market

Gilmartin observed the productivity losses caused by the lack of functional co-ordination in bringing a drug to market. Having worked with the consulting firm PRTM at Becton Dickinson, in 1995, he suggested that they be brought in to help streamline the drug development process. This resulted in the implementation of the Product and Cycle Time Excellence (PACE) process, a best-practices protocol for communication between MRL, manufacturing and marketing during the drug development process. The aim was to bring products to market more quickly, and with better clinical, economic and commercial profiles.

The PACE process is activated when a drug enters late-stage development in Phase II b-III, the most intensive phase, comprising of double-blind large-population human testing, safety in long-

term use, and comparison against selected competitive drugs. This phase culminates in the New Drug Application submitted to the FDA. PACE is a stage-review process that specifies the order and interleaving of research, marketing and manufacturing plans and milestones to ensure that the information, materials and other resources required for positioning the drug are available to all relevant groups in a timely manner. A master product development plan is generated for each drug under development, and a senior-level Product Approval Committee oversees its implementation. "Contract breaks" (deviations from plan), are identified at interim reviews, and recovery or a plan change is discussed.

While PACE did not change the nature of activities within in each functional area, it greatly increased the information flow between functions. This led to significantly better planning and more rapid product launches. David Anstice said: "PACE brought order to the dialog between MRL and marketing." Ed Scolnick, head of MRL commented:

> When Ray came to Merck, research, marketing and manufacturing were not tightly coupled. They always went to the internal research review (run by research), but their interactions were not in lock step. So scale operations were not well done. . . . Then, we instituted the PACE process. It has been effective. Time to market has improved. There is less friction with marketing, the label is ready when R&D hands over the drug, manufacturing can offer it in a matter of days.

A New Marketing

David Anstice, President of U.S. Human Health, had long recognized the need for lifecycle-oriented franchise management to effectively counter competition from therapeutically equivalent drugs. He now re-organized marketing in the U.S. into Franchise Business Groups (FBGs), with each taking P&L responsibility for Merck's products in a given therapeutic area such as osteoporosis, respiratory diseases, etc. (see **Exhibit 8b**). Similarly, under Per Wold-Olsen, the country marketing organizations outside the U.S. started to evolve away from traditional marketing and sales functions, to ones that focused on therapeutic franchise management, with each therapeutic area adopting a strategic agenda that linked MRL, marketing and manufacturing.

As Merck elevated the marketing organization and linked the inputs it required into the PACE process, Gilmartin set about strengthening skills inside marketing. Monitor Consulting was hired to help develop tools to steer the marketing function away from its usual "industrial marketing" style towards consumer or brand marketing. The Merck marketing staff was trained in data-driven methodologies and analytical approaches such as buyer segmentation and customer decision-making maps. Web-based marketing tools were designed and integrated into the PACE process. Those tools were also made part of a marketing curriculum that all people in the marketing function were expected to get trained on and integrate into their day-to-day analyses and planning processes. The aim was to make marketing a more professional discipline at Merck, and to help each marketing staff person envision a career path leading up to a position of line responsibility, such as head of an FBG.

A staff executive described the changes: "In the past, people would wander into marketing. The new marketing now required people to get experience in specific marketing functions such as brand management, advertising, product development, etc., and have their career trajectory tied to specific skills, sort of like getting their PhD in marketing." The creation of the FBGs added a layer of marketing jobs with strategic and line responsibility for specific therapeutic groups and provided meaningful career paths for ambitious marketing employees. It also resulted in a more scalable marketing organization—new products could be added to existing franchises, or new franchises could be created as Merck entered new therapeutic areas.

Working Together on Strategy

Gilmartin saw that loyalty and excellence within the functions also highlighted differences between them. He decided to link the functions with cross-functional organizational structures that would focus on franchise strategies and their implementation. In 1995, he instituted WBSTs or Worldwide Business Strategy Teams for each therapeutic franchise group. Each WBST, consisting of 12 to 15 members, had a core franchise team composed of a senior person from each of U.S. Human Health, worldwide marketing, and MRL's regulatory and clinical groups. The WBST work of its team members was to be consistent with their functional jobs and they were to run the franchise like an independent business. Although the PACE process was in place as a mechanism for overseeing product development, the WBSTs were envisioned as serving a different purpose: they were seen as the focal point for Merck's efforts to manage the therapeutic franchises on a global basis.[19] Each WBST would drive the development and implementation of franchise strategies.

A WBST may, for example, discuss an ongoing Phase V study, with the MRL representatives on the team presenting the status of the study, its likely outcomes and their implications. If the results of the study were likely to be positive, the WBST would discuss dissemination of the information on the drug label and within the medical community, the expected impact on sales, and manufacturing's ability to handle any anticipated demand surge. If, on the other hand, the results were likely to be negative, the discussion would focus on communicating the results to the medical community, effective management of the impact on the drug label, the public affairs issues, investor relations and strategic options to limit competitive damage. The WBST members would return to their functions to collect information and request specific actions, and then report back to the WBST. The head of each WBST also met separately with Gilmartin's Management Committee to provide regular updates on their therapeutic area.

When WBSTs were first introduced, some team members displayed an uneven commitment and action-orientation. For example, issues would surface at the meetings, but the required follow-through would not necessarily occur in the designated functional areas. Often this would be accepted as inevitable, since the early WBSTs had little clout and were not initially held accountable for results. Part of the challenge was that the WBST leaders did not have any direct decision authority, but they were asked to provide leadership in managing the therapeutic franchise

However, some WBSTs, particularly those with strong leaders, became very effective in working with the various functions to position, promote and get resources for their category's drugs, and they started to earn the respect of the larger organization, particularly MRL. Gilmartin commented, "The design and function of WBSTs was initially agonizing, but there has been lots of continuous improvement." Members of effective WBSTs facilitated the handling of franchise issues within their respective functions. Over time, some WBSTs got better at proposing strategy and pushing for new product initiatives. Gilmartin cited an example of WBST effectiveness: *Proscar*, a drug for the treatment of enlarged prostate, had originally been sidelined, but due to the initiative of the Urology WBST, more and better outcome studies were conducted, and *Proscar* had resumed 15-20% growth in the late 1990s.

Funding Phase V Research

By the mid-1990s, there were a plethora of breakthrough drugs available to treat several large-population diseases. Each disease could be treated via multiple pathways and each pathway could

[19] Johnson & Johnson, for example, epitomized the opposite approach to cross-functional cooperation. It was organized by therapeutic divisions with complete P&L responsibility for each of their franchises.

be treated with multiple drugs from different companies. Physicians and MCOs, who jointly determined the prescribing of drugs, were increasingly demanding outcomes information in order to choose between otherwise similar options. For example, for the treatment of arthritis, they were faced with the choice between cox inhibitors and naproxen; within cox inhibitors, they had to choose between Merck's *Vioxx*® and Pfizer's *Celebrex*®. Phase V studies, by focusing on outcomes, were beginning to have a huge impact on the life-cycle revenues of blockbuster drugs. But, Phase V studies also historically had created tensions for MRL, which preferred to apply its limited R&D resources, mainly human capital and funding for outside investigators, to the development and registration of new drugs.

When Gilmartin came to Merck, clinical development groups had been established as Phase V research groups within marketing, but all clinical research, including Phase V, had to be approved and funded through MRL.[20] With the advent of the WBSTs, a new path was created within the organization for proposing outcome studies and getting them approved. For example, the field sales force or the marketing group for a particular drug may envision the need for a Phase V study; they could then petition the appropriate WBST, which would take up the case: the cross-functional team members would analyze and establish the need for the Phase V study and outline relevant study parameters, including timing and necessary funding.

Beginning in 1997, the Product Approval Committee met regularly to review all of the clinical studies proposed via the WBSTs for drugs in late-stage development or for drugs already on the market. Based on available research capacity, market considerations and expertise, Phase V clinical studies would be assigned to MRL, or to the clinical development groups in marketing. The clinical development groups in marketing would have their own dedicated budgets to conduct clinical studies and could conduct critical Phase V studies. To ensure quality and scientific validity, each and every clinical research study protocol was still vetted at the start and at periodic reviews by the Clinical Research Review Committee (CRRC) which was part of MRL. Expressing satisfaction at marketing's new-found ability to initiate and run their own clinical after-market studies, a marketing executive said, "The CRRC can comment on the science of a study, but not on the business case."

A prime example of the success of this new approach was a marketing-initiated Phase V study, "*Losartan* Intervention For Endpoint Reduction," or LIFE study, conducted on *Cozaar*®, Merck's blockbuster drug for hypertension or high blood pressure. The study was launched by the clinical development groups in May 1995, to study the impact of *Losartan* on overall morbidity rates.[21] From mid-1995 to mid-1997, 9,200 patients were enrolled in the study, and they were followed through September 2001. As reported in a March 2002 article in the journal *Lancet*, LIFE established that *Losartan's* specific mechanism for blocking Angiotensin II in the body reduced cardiovascular morbidity rates in hypertensive patients, and was particularly effective in reducing cardiovascular morbidity in hypertensive diabetic patients who face the additional risk of heart muscle damage. On March 21, 2002, *The Wall Street Journa*l reported:

> Merck & Co. has scored a win in a head-to-head test that showed its hot-selling blood-pressure medicine *Cozaar* is markedly better at preventing strokes and diabetes in patients with high blood pressure than an older, commonly prescribed medicine called *atenolol*. . . . The

[20] As a point of contrast, Pfizer located all responsibility, resources and decision-making authority for after-market clinical studies (Phase IV studies at Pfizer), within its marketing function.

[21] While the efficacy of *Losartan* in blocking the enzyme Angiotensin II and thereby lowering blood pressure was well accepted, death rates for hypertensive patients treated with the drug remained very high, relative to non-hypertensive patients. Doctors and MCOs were requiring outcome efficacy, i.e., death rate reduction, before prescribing the drug or putting it on a formulary.

> results are likely to influence doctors'—and perhaps insurance companies'—drug preferences and could transform the market for blood-pressure drugs.

Earlier, Per Wold-Olsen and other marketing managers had often faced an uphill task in trying to get MRL to design and run Phase V outcome studies. Now, with the increased role of marketing managers, the involvement of the WBST, and a dedicated budget for the clinical development groups, the Product Approval Committee could agree on a franchise strategy and approve new studies across MRL and the clinical development groups to support the strategy. A senior marketing executive commented, "Unlike the 4S study, nobody had to lay his life on the line to get the *Cozaar* LIFE study done. In the olden days, we couldn't ask for Phase V studies; then, we could ask, but we got booted out; after that, we could ask, and sometimes MRL did it; but now, we have the resources—we are doing our own label-change studies!"

Forging External Relationships

In a July 2000 memo to his senior managers Ray Gilmartin called for an increased emphasis on external partnerships to maintain Merck's lead in cutting-edge science. He formally aligned the corporate staff group responsible for external collaborations with the Worldwide Licensing group within MRL, and put Dr. Ben Shapiro, a 10-year MRL veteran, in charge (see **Exhibit 8b**). The existence of this joint group, charged with evaluating new technologies and handling licensing and other collaborative arrangements, made it easier for external parties to deal with Merck. It was integrated with MRL and could call upon scientists, strategists, financial analysts and deal makers as needed.

Gilmartin and Shapiro pointed out that working with external partners was not new to Merck. Even before the formation of Shapiro's group, almost a third of Merck's sales came from drugs like *Fosamax*® and *Cozaar* that had been discovered outside and developed within Merck. But Ben Shapiro explained how the orientation was changing:

> There was always a psychological resistance to external research (from MRL). But now, 99% of biomedical research is outside of Merck. So, we must pick the best of what is out there and bring it back so that MRL scientists can influence all of the global research in an area. Ray Gilmartin, Judy Lewent (CFO) and the Management Committee have, by setting up a separate budget, eliminated the either-or choices that researchers had had to make about inside-outside research.

Gilmartin echoed these ideas: "Basically, as before, MRL has first call on Merck's dollar. What has changed since 2000 is our view of external opportunities . . . so we decided to set aside corporate dollars, not MRL dollars, for *scientific opportunity exploration*—not just business licensing and joint ventures."

Senior scientists at MRL took pride in their "taste function"—their ability to recognize good science and to estimate the scientific value and risk of a new molecule or technology, and the Worldwide Licensing group was well-positioned to leverage that talent. For example, in the summer of 2001, after less than a month of deliberation and negotiations, Merck acquired Rosetta Inpharmatics for $620 million.[22] Explaining Merck's preference for early-stage collaborations and the Rosetta decision, Ben Shapiro said, "We would never do what Pfizer did with *Lipitor*—just buy the

[22] Founded in December 1996, Rosetta was an early leader in gene expression analysis. Its technology solutions, including the Rosetta Resolver system, were designed to accelerate drug discovery by improving biological data analysis. (Rosetta business description extracted from the May 11, 2001 *Business Wire* on global.factiva.com.)

completely finished drug. They ended up having to buy Warner Lambert when they did not want to. What we look for are product candidates. The Rosetta acquisition was like a "PC upgrade." It will improve our platform technologies, increase the number of compounds that come up, and increase the hit rate."

Looking Ahead

Ray Gilmartin could point to many changes at Merck over the past seven years, recounting that when the PACE process was first instituted and WBSTs were first formed, there were some in *marketing* who felt most threatened by the transparency of the process. He felt that the marketing organization had since become much stronger, confident and able to leverage cross-functional resources to maximize the value of each franchise group. He explained "In the 1990s, if you were a great marketer, you wouldn't have come to Merck, and we wouldn't have hired you, but Merck is now successfully recruiting marketing personnel from industry and from the best business schools."

Further, MRL had embraced the role of maximizing the marketing value of the drug label. Even Ed Scolnick, who had historically resisted outcome studies as a poor use of limited research resources, had recently been known to express concern about the marketability of a drug from a potential partner company that "didn't think through the trials well enough to have a strong label for the marketing people to sell." MRL researchers often participated in customer focus groups, trying to improve their understanding of lifestyle and compliance issues that had a bearing on drug development. By 2002, Merck's formally stated strategy was: "Turning cutting-edge science into novel medicines that are true advances in patient care, with proven clinical outcomes." [23]

Merck's efforts had led to many tangible improvements. The marketing organization was at the discussion table for all major decisions, their input was sought proactively and it was getting easier to hire talented professionals eager to pursue a career in marketing at Merck. It was estimated that PACE and other process improvements at MRL had led to a significant reduction in drug development time, sometimes by as much as 12 months. Some of the WBSTs had been very effective in managing their therapeutic franchises and there was a consensus that Merck was now better-positioned to defend its product categories and to anticipate regulatory and competitive issues. Several significant Phase V studies had had a major positive effect on drug labels, patents and sales, and indeed, outcomes research had become a part of Merck's stated strategy. A senior marketing team member pointed out, "Today, if we have a new compound and want to do a 4S type of study, it would not depend on the persistence of some stubborn Scandinavians, it would be handled within the PACE and WBST process . . . we always had the knowledge and skills, now we have the proper processes in place, too."

Still, problems remained. Gilmartin had resisted changing the fundamental functional structure of the company and had particularly avoided creating formal lines of hierarchical control between the WBSTs and the functions. Since membership to a WBST was added on to one's usual responsibilities, it was viewed by some as a sideline task. Even the head of a WBST viewed as effective and successful described it this way: "As the head of a WBST . . . I have no ultimate responsibility or decision-making authority. The WBST itself has no decision-making power, but the people on the team have power within their functional organizations." As a result, there was a lot of variation in the effectiveness of different WBSTs. Top management wanted WBST members to express greater ownership of the therapeutic areas and to pursue issues and solve problems more energetically.

[23] Ray Gilmartin's presentation to analysts December 2002 and internal company communications.

Also, some WBST leaders felt that despite the enhanced role of WBSTs, they held only modest clout with MRL. Since MRL was organized into discovery, preclinical and drug development phases (and within those, by academic specialties), it sometimes was hard to identify a researcher who would take responsibility for a specific franchise-related research issue that might come up in the WBST.[24] Also, some tension emanated from the fact that the allocation of resources to a drug by MRL was greatest in Phase II and III and ramped down after registration, whereas marketing felt that successful franchise management required continued intensive research attention, starting at the end of Phase III, with the launch of the drug, right through Phase V after-market studies.

Some areas in MRL were also very hierarchical, and sometimes, the MRL person on a WBST would have to discuss issues with three or four layers of MRL management to get the resources needed to solve a problem. In contrast, marketing had established a direct reporting relationship between franchise heads and a President of Human Health or an EVP of Worldwide Human Health Marketing, and this enabled very prompt resolution of matters related to marketing the franchise.

In 2002, Ray Gilmartin and his management committee were implementing an initiative to address the issue of WBST performance management. The proposal called for the WBSTs to adopt performance grids similar to those in place for the line organizations, using a 100-point scale for planned performance measurement. The plan allocated 20% of the score for financial goals such as sales and growth metrics, 10% for leadership effectiveness and 70% for strategic measures such as progress on strategic projects, market share, competitive response, etc. A group score would be estimated for each WBST and it would be factored, with a weight ranging from 5% to 25%, into each team member's overall performance evaluation.

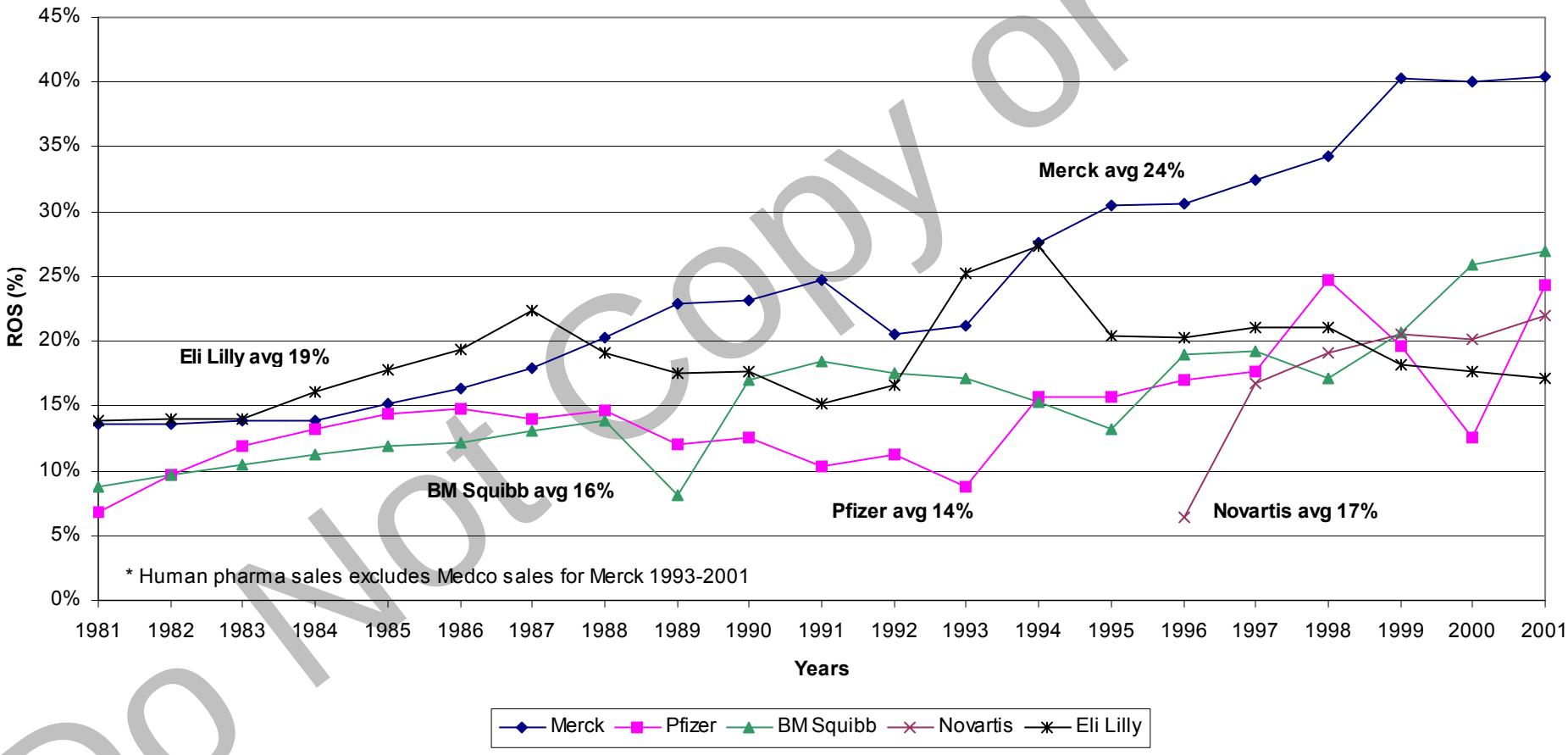
However, there were concerns that some of these efforts went too far. Should scientists working on clinical trials be rewarded financially for their drugs' performance in the marketplace or did this create conflict with their clinical responsibilities? Would a strong focus on the therapeutic franchise come at the cost of Merck's scientific focus and identity? Would a growing commitment to Phase V outcome studies and MRL responsibilities in the franchises limit Merck's ability to recruit top scientific talent?

The dual challenges of hitting peak annual financial performance while keeping the research pipeline full continued to weigh on senior management. Gilmartin wondered, "What actions should we take at this point? Have we gone far enough? How far can we progress and still preserve Merck's distinctive science-led culture?"

[24] An alternative model for a pharmaceutical research organization, one that had recently been adopted at Novartis, was to be organized along therapeutic lines in a decentralized structure.

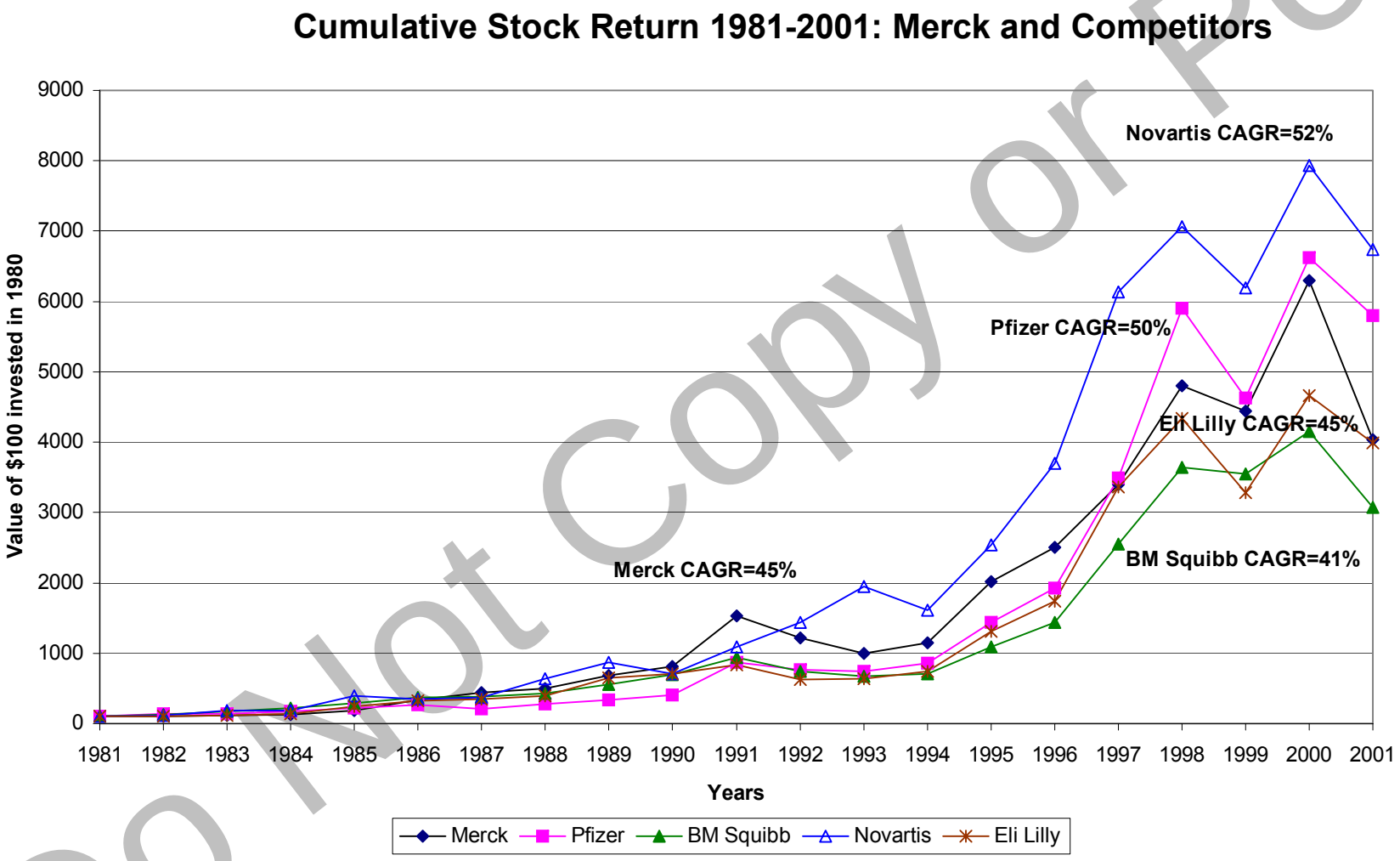
Exhibit 1a

Return on Human Pharma Sales* 1981-2001: Merck and Competitors



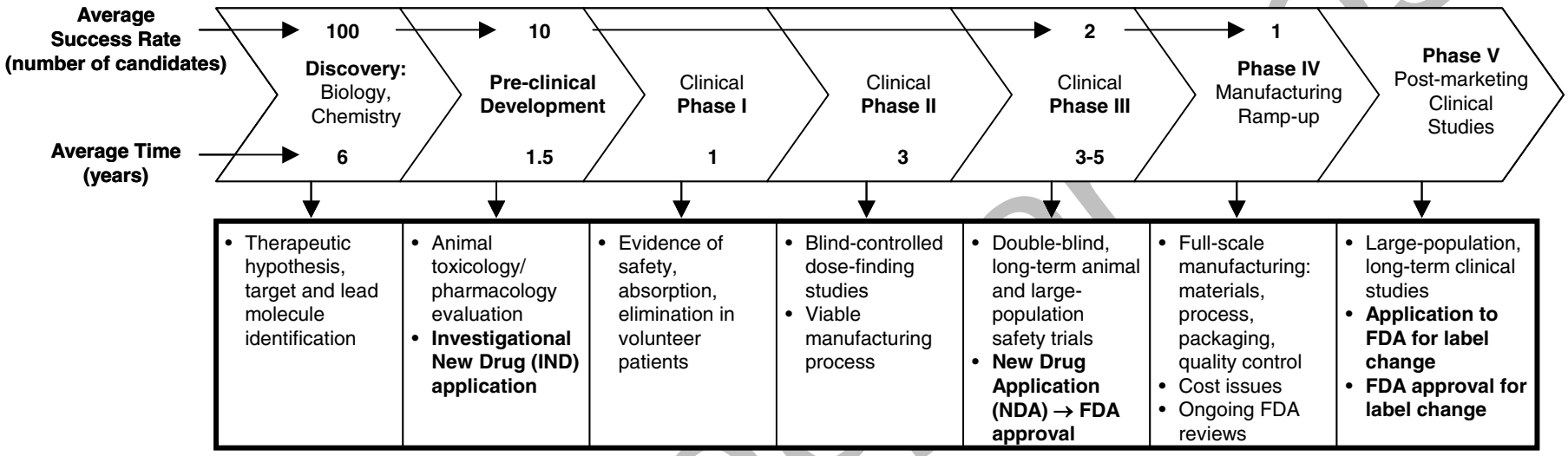
Source: Standard & Poor's Compustat® data, accessed Feb 2003 and HBS casewriter analysis.

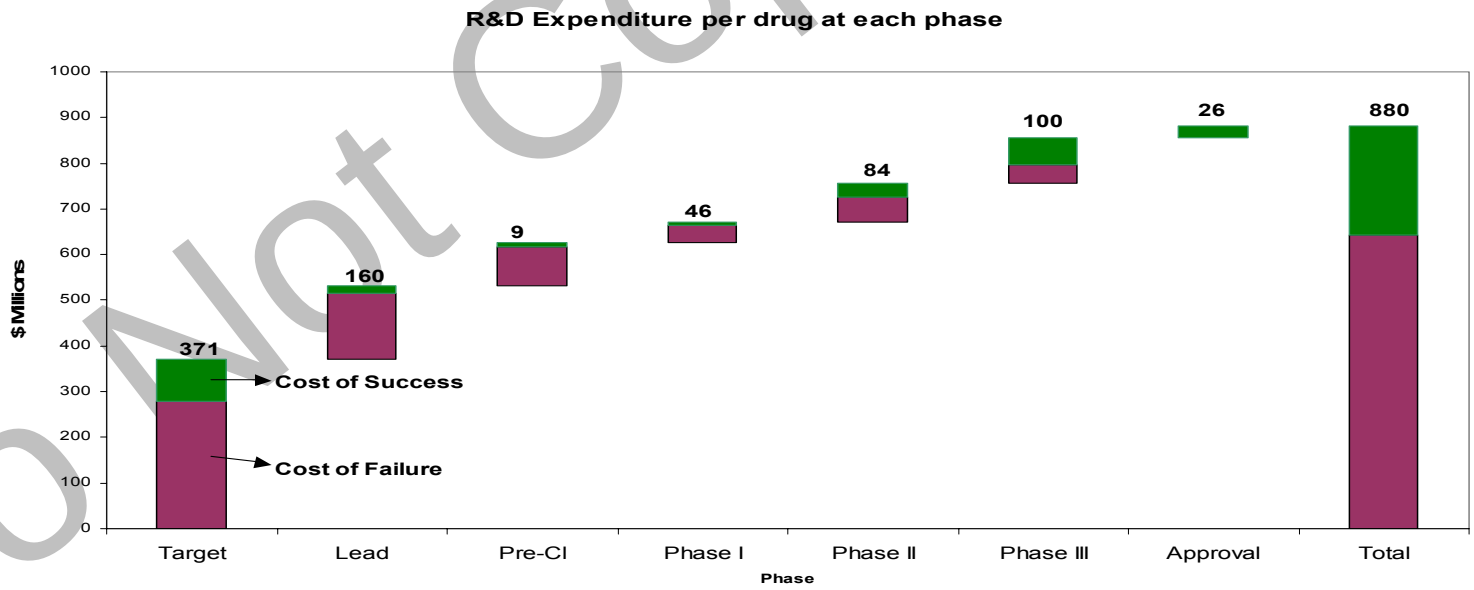
Exhibit 1b



Source: CRSP and Thomson Datastream data accessed February 2003, and HBS casewriter analysis.

Exhibit 2





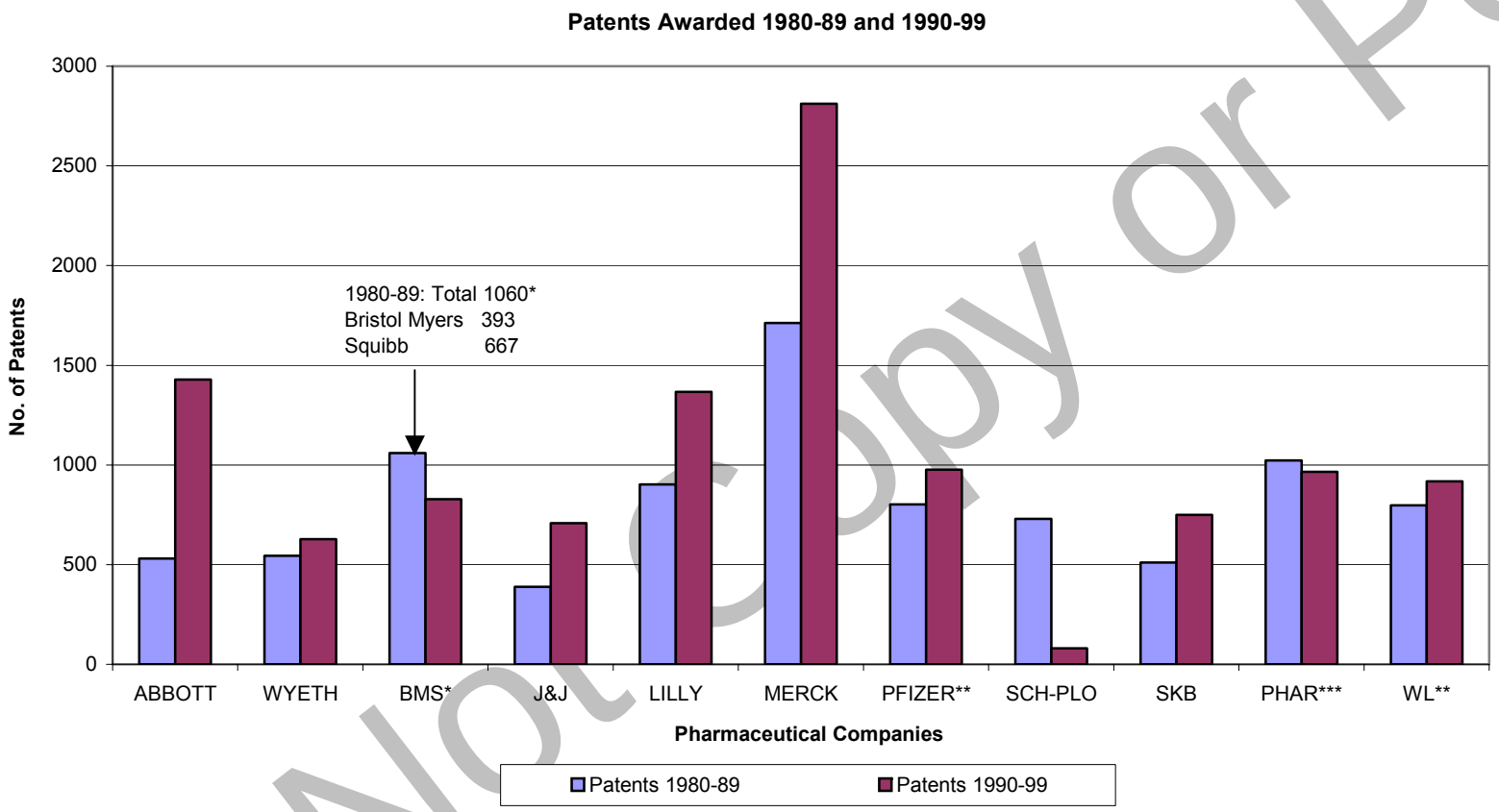
Source: Boston Consulting Group report, "A Revolution in R&D: How Genomics and Genetics are Transforming the Biopharmaceutical Industry," November 2001; Report from the Tufts Center for the Study of Drug Development, http://csdd.tufts.edu, accessed November 2001 and interviews with Merck research directors.

Exhibit 3 Selected Product Line Sales and Profits for Major Pharmaceutical Companies

Company	Product Category	2001 Sales ($ millions)	2001 Profits ($ millions)
Abbott Laboratories	Pharmaceuticals	3,759	1,409
	Diagnostics	2,929	357
	Hospital products	2,778	738
GlaxoSmithKline	Pharmaceuticals	24,775	8,716
	Consumer healthcare	4,729	
Johnson & Johnson	Consumer products	6,962	1,004
	Pharmaceuticals	14,851	4,928
	Professional products	11,191	2,001
Lilly (Eli)	Life-sciences products	11,542	2,809
Merck	Human health management	19,732	12,200
	Prescription and health management	29,693	731
	Animal health and other	1,266	978
Pfizer	Prescription pharmaceuticals	26,949	10,936
	Other pharmaceuticals	5,130	787
Pharmada	Pharmaceuticals	11,970	1,291
	Agricultural	1,867	
Schering-Plough	Pharmaceuticals	8,369	2,523
	Healthcare products	739	
	Animal health	694	
Wyeth	Pharmaceuticals	11,717	3,504
	Healthcare products	2,412	592

Source: S&P Industry Survey at www.netadvantage.standardandpoor.com, accessed March 2003.

Exhibit 4a



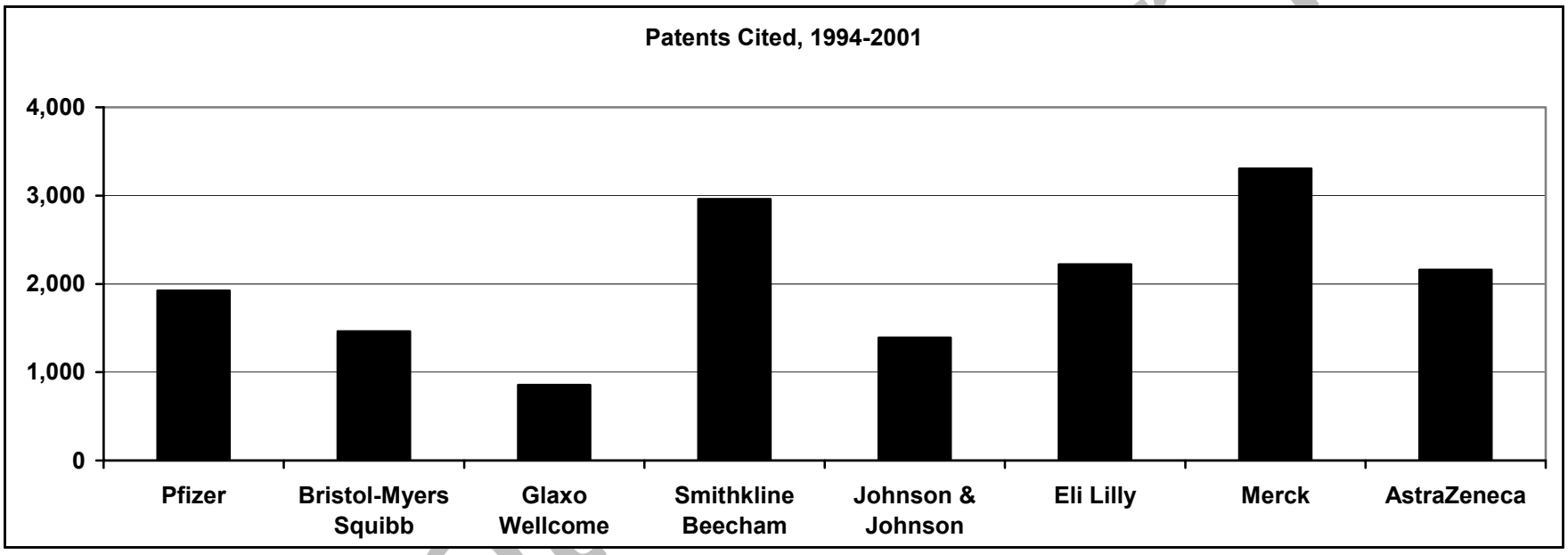
Source: U.S. Patent and Trademark Office, www.uspto.gov accessed November 25, 2002.

*Bristol Myers merged with Squibb in October 1989. 1980–1989 number combines patents for the two companies, 1990–1999 number is for merged company.

**Subsequently, Pfizer acquired Warner Lambert (WL) in hostile takeover, effective June 2000.

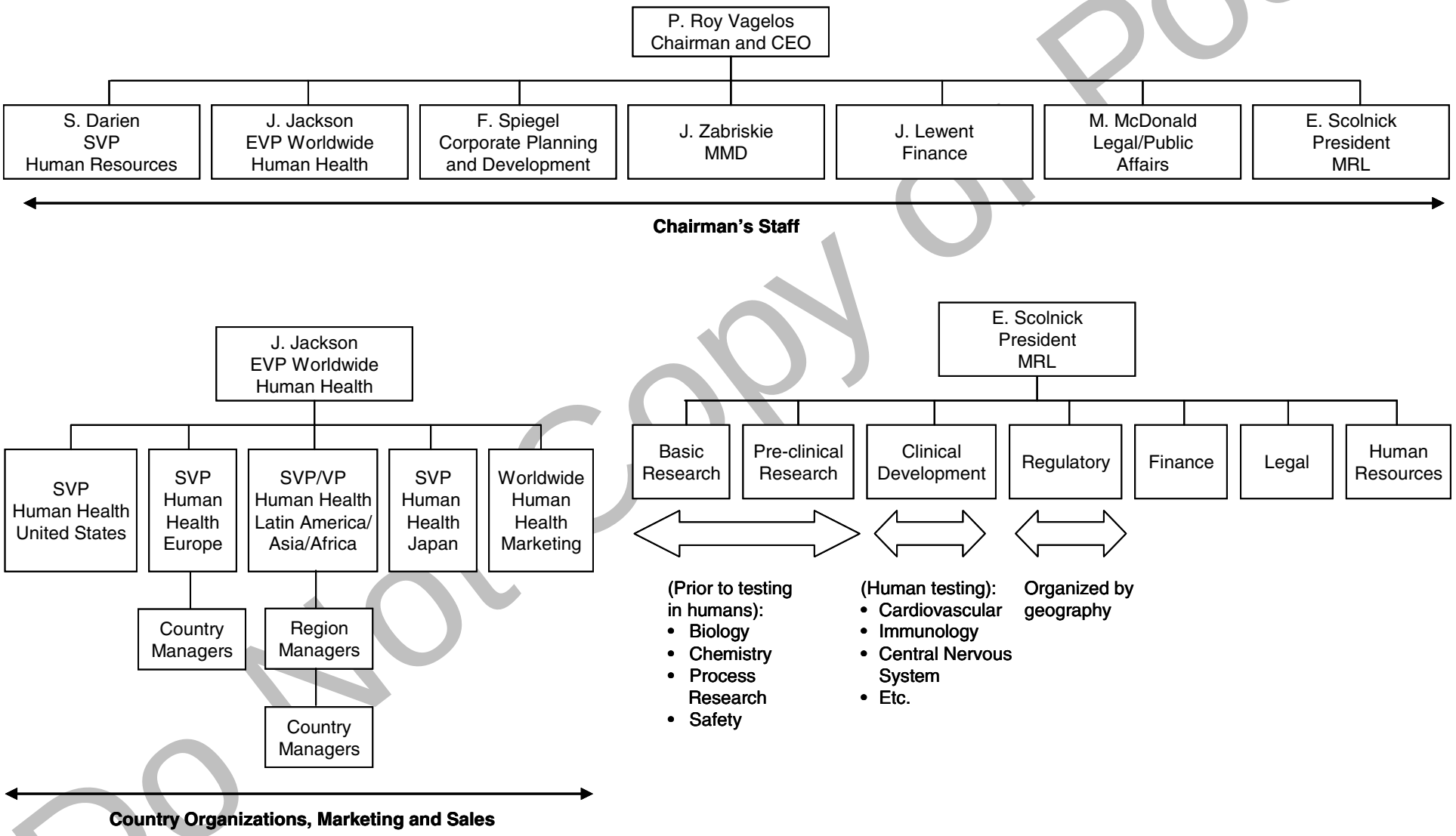
***Pharmacia merged with Upjohn in November 1995: 1990–1999 numbers include combined company.

Exhibit 4b



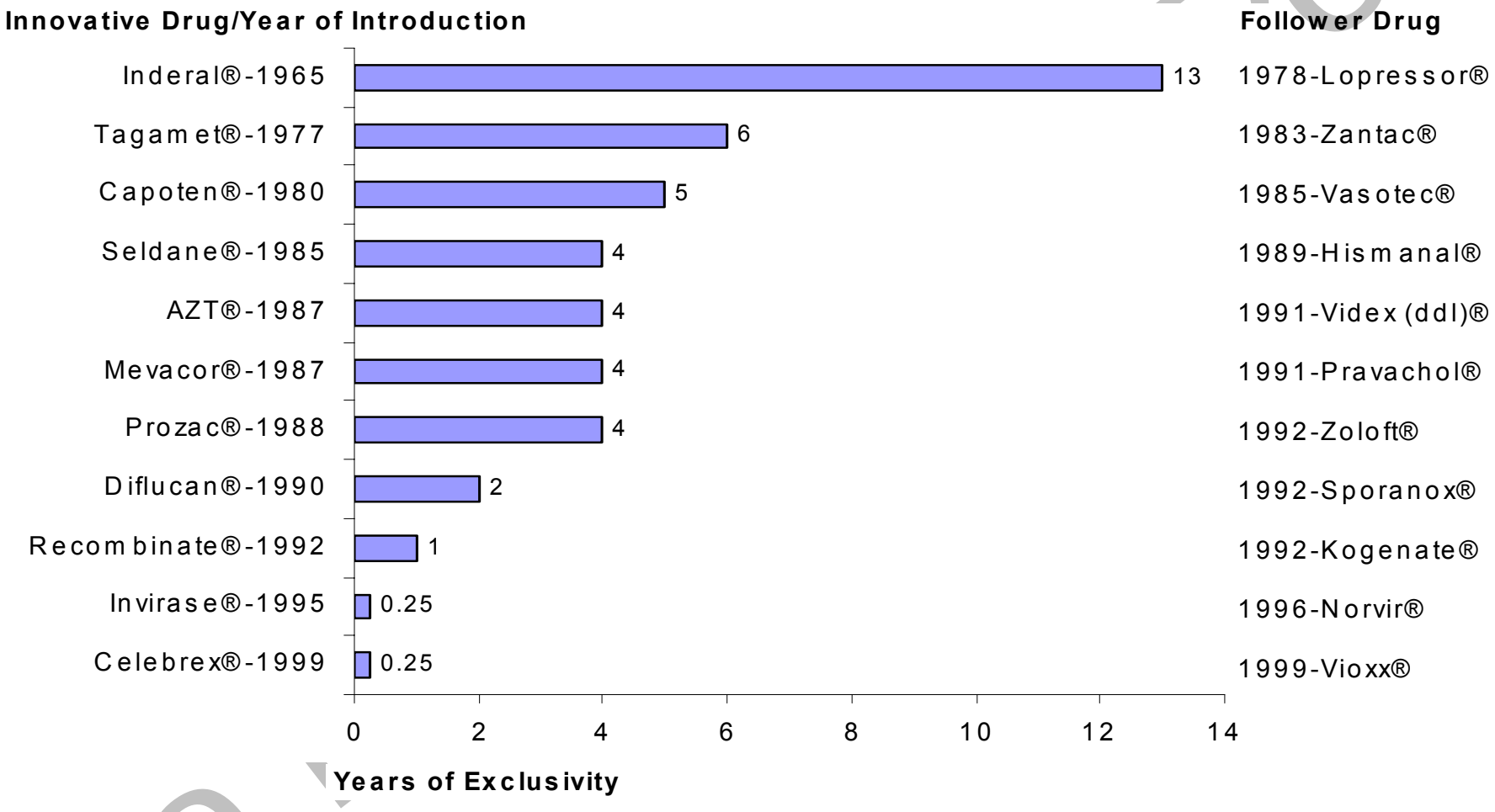
Source: IFI/Plenum, accessed November 25, 2002.

Exhibit 5 Vagelos' Organization Chart, June 1993



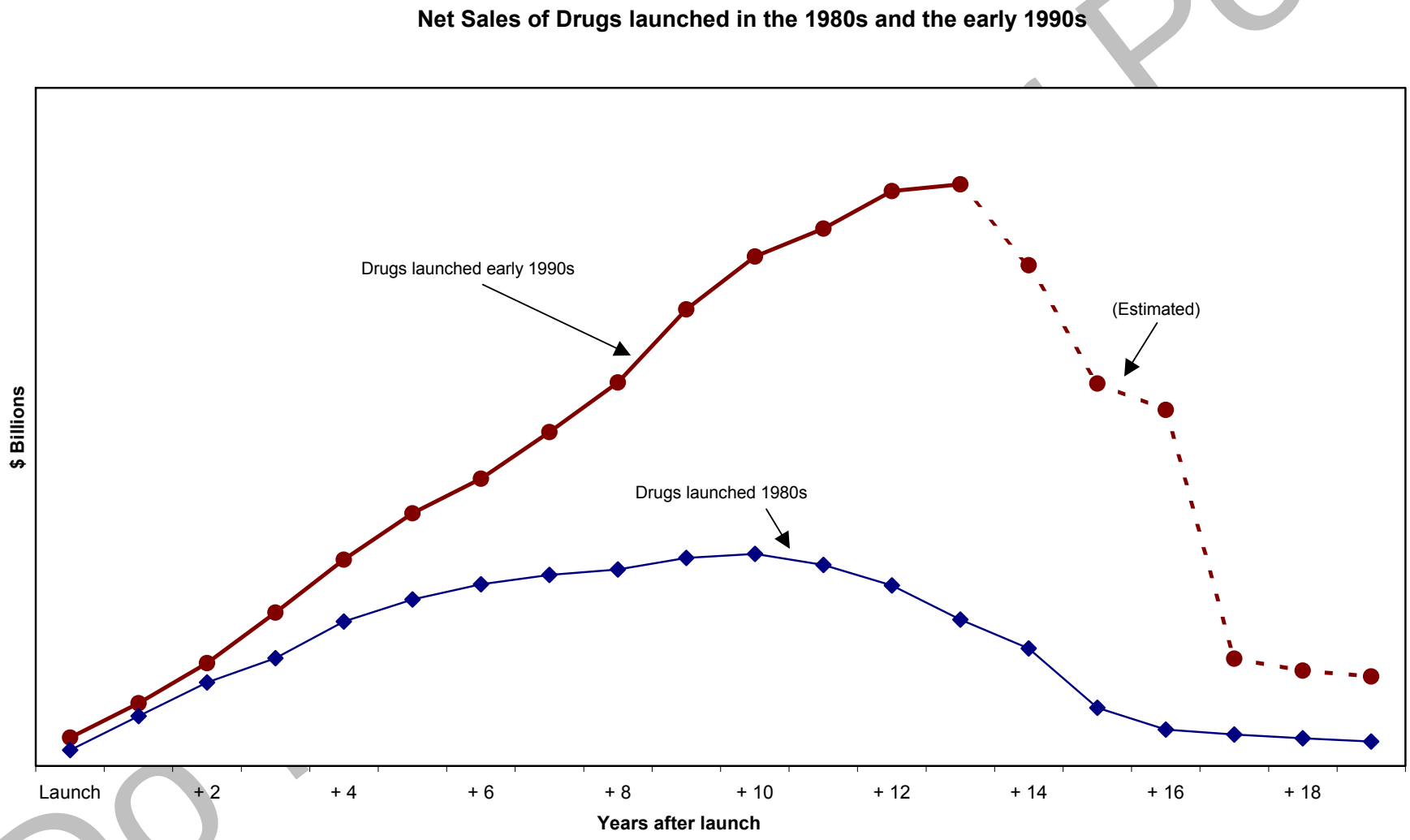
Source: Company documents.

Exhibit 6 Typical Product Exclusivity Patterns 1960s – 1990s



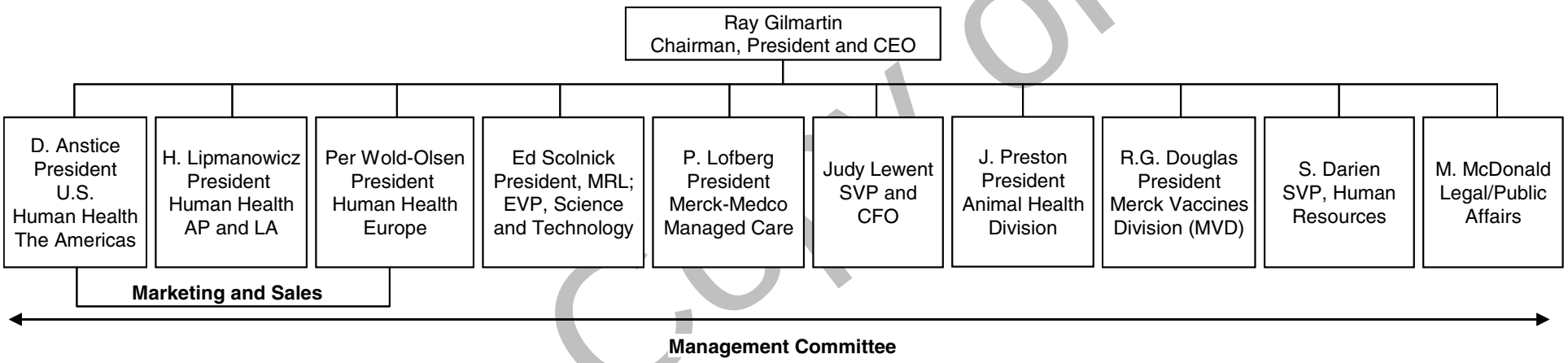
Source: PhRMA, 2000; The Wilkerson Group, 1995, as reported in Pharmaceutical Research and Manufacturers of America, *2002 Industry Profile*, PhRMA, Washington, DC, 2002, p. 33.

Exhibit 7



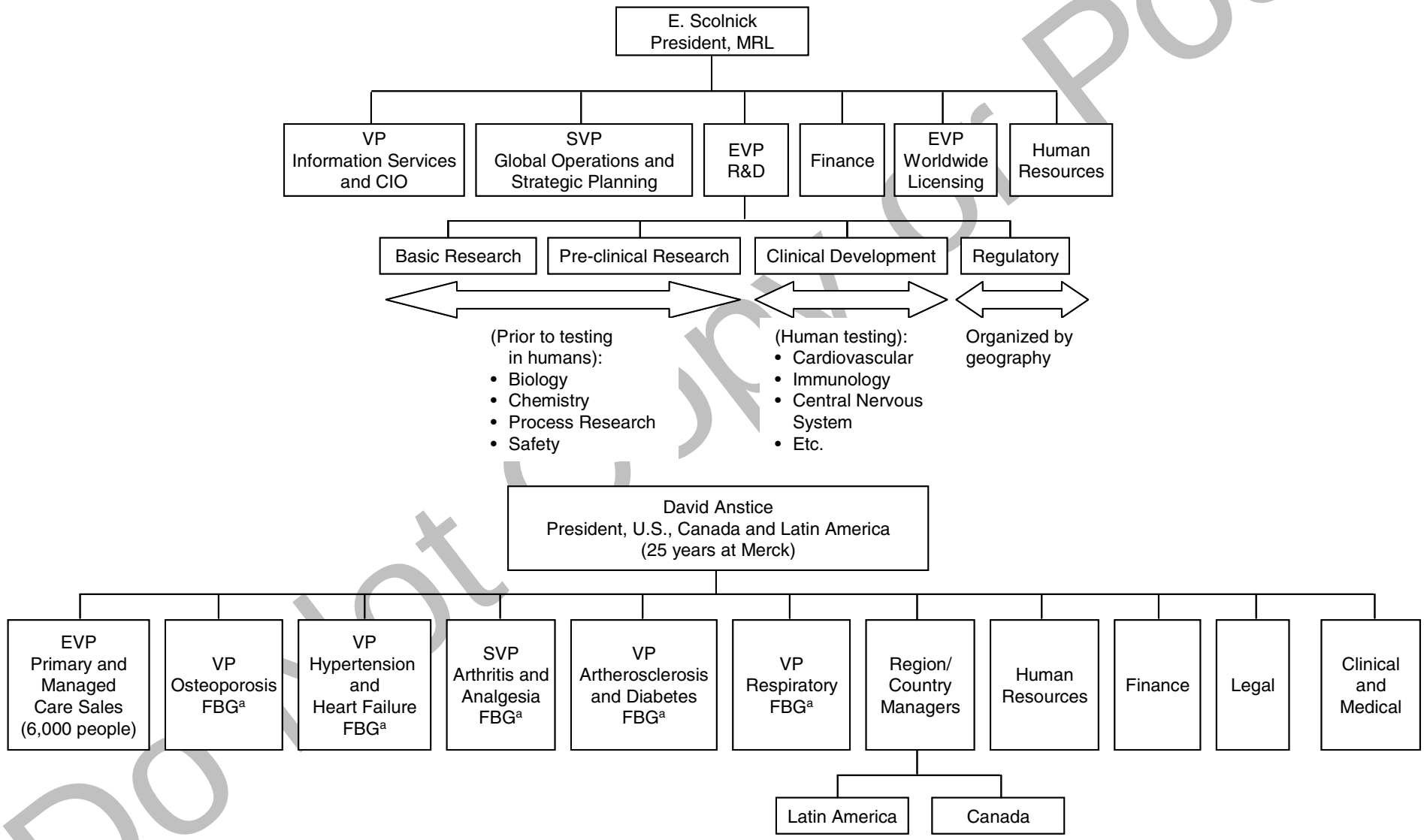
Source: Company analysis.

Exhibit 8a Ray Gilmartin's Management Committee, September 1994



Source: Company documents.

Exhibit 8b Research and Marketing (U.S. Human Health) Organizations, September 2000



Source: Company documents.

[a]Franchise Business Group.