INDIAN PHARMACEUTICAL INDUSTRY: CHALLENGES AHEAD

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An attempt has been made in this article to develop a path to build a global pharmaceutical brand based on the understanding of the numerous complex issues that currently face the Indian pharmaceutical industry.

I. OVERVIEW

India's healthcare spending is roughly 6 percent of GDP of which almost three fourth is spent from private resources. By comparison the health-care spending in the USA is about 11 percent of GDP, majority of which is from government or third party (insurance) funds. The expenditure on medicines is roughly 16 percent of all healthcare spending. It is important to keep in mind that there are several systems of medicine in use both traditional and modern. In this note we cover the modern sector, which largely consists of allopathic prescription drugs and formulations. The pharmaceuticals industry in India evolved from being almost non-existent before 1970 to a prominent provider of healthcare products, meeting 95 percent of the country's pharmaceuticals needs. The size of the Indian pharmaceutical industry has increased from INR 4 billion in FY71 to INR 197.4 billion in FY00, which is a compound annual growth rate of 16.4 per cent per annum. The total Indian production constitutes about 1.3 percent of the world market in value terms, and 8 percent in volume terms. This is because drug prices in India are about 1/6th of average world prices. The industry is a net foreign exchange earner with exports of bulk drugs and finished formulations, amounting to INR 70 billion in FY00, and the biggest market for Indian pharmaceuticals is USA. Per capita consumption of drugs in

India at USD 3 is amongst the lowest in the world compared to Japan's USD 412, Germany's USD 222 and USA's USD 191.

The pharmaceuticals industry can be divided into two segments : *Bulk Drugs* which are the active ingredients with medicinal properties and are the basic raw materials for making formu-lations and *Formulations* which are specific dosage forms of a bulk drug or of a combination of different bulk drugs and the final form in which the drugs are sold i.e. syrups, injections, tablets and capsules. With the objective of controlling prices of important drugs and making them available at reasonable rates to the consumer, the Government introduced the Drug Price Control Order (DPCO) in 1970. It

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specifies the maximum selling price of bulk drugs and formulations and the turnover ceiling for exemption from the DPCO. At present DPCO fixes and monitors the prices of 74 bulk drugs, and all the formulations manufactured using any of these bulk drugs thus covering 50 percent of the pharmaceuticals market. DPCO has been amended with three revisions in 1979, 1987 and 1995. The number of drugs under price control has been reduced with every revision.

The Government also enacted the Indian Patent Act (IPA) in 1970. Unlike the international norms, this Act provided for process patents, which recognized the process to manufacture a product and not the end product. This move was intended to develop the indigenous pharmaceutical industry. Indian companies took advantage of this policy and succeeded in producing molecules by reverse engineering, which were under patent protection elsewhere, at a cost that was a fraction of the original research cost. This cost advantage allowed Indian companies to price their products considerably lower as compared with their international counterparts. This scenario is going to change as India being a member to the World Trade Organization (WTO) is bound to introduce the patent regime and provide legal protection to Trade Related Intellectual Property Rights (TRIPS) by January 1st, 2005. This would provide patent protection for new products and Indian industry would no longer be able produce patented drugs at will and market them without license from the patentee. Till such time that the patent law becomes applicable Exclusive Marketing Rights (EMRs) have been granted to foreign manufacturers for five years.

The noteworthy features of the Indian Pharma Industry are immense flexibility in the industry to move from one drug to another with ability to respond quickly to new demands and needs, strong distribution networks with strong presence in the foreign markets (net exporter of bulk drugs & formulations), advantage of low production and R&D costs as compared to other nations and availability of high skills in process development, low R&D expenditure by Indian manufacturers mainly due to relative small size and resource base of individual units compared to major international pharma companies limiting R&D options, world class manufacturing plants approved by US-FDA, and low profit margins as it is a highly fragmented industry with intensive competition.

II. STRUCTURE OF THE INDUSTRY

The pharma industry in India is highly fragmented both in terms of number of manufacturers, with over 23,000 licensed units as well as the variety of products. Out of these 23,000, there are about 250 large units and more than 8,000 small and medium scale units which form the core of the industry. The industry has a wide range of over 100,000 drugs (which includes vitamins, antibiotics, antibacterials, cardio-vascular drugs etc.) and nearly

80 percent of the manufacturers have sales less than INR 1 billion. The top five companies in the industry - Ranbaxy, Glaxo, Lupin, Hoechst and Cipla account for only 19 percent of the industry's turnover, and the top ten control around 31 percent of the market. All the players focus on limited number of product groups and try to achieve strong presence in them.

Geographically, there is a concentration of manufacturing operations in three states of Maharashtra (more for pharmaceuticals formulations than bulk drugs), Gujarat (more for bulk drugs) and Andhra Pradesh (also for bulk drugs).

Government policy as well as the regulatory framework has been the primary reason for the fragmentation. The combined effect of the IPA and the DPCO resulted in a highly fragmented structure. The lack of product patents enabled manufacturers to produce existing drugs through alternate processes. This has resulted in low capital requirements reducing the level of entry barriers to a bare minimum and more than 80 percent of the companies have assets of less than INR 1 billion. Besides, the exemption of payment of excise duty by small scale units and their exclusion from the DPCO further led to their proliferation as it helped them in enjoying very low overheads. The Pharma Industry can be broadly divided into Organized and Unorganized sectors. There are around 300 manufacturing and formulation units in the organized sector and it accounts for 70 percent of the total sales of the industry. Around 100 players in the organized sector account for about 90 percent of the total industry turnover. The market is concentrated at the top with the top 30 players controlling about 70 percent of the market share. Moreover, the growth rate of the top 30 players is around 18 percent per annum as compared with the industry growth rate of about 15 percent. The organized sector can be classified into Multinational companies (MNCs) and Indian companies on the basis of management control. The MNCs, which had dominated the industry till 1970, began to lose market share following the failure of the IPA to recognize product patents. The share of multinational companies declined from about 90 percent in 1970 to about 20 percent in 2000. Consequently, the market share of the Indian companies increased steadily from low levels of about 10 percent in 1970 to over 80 percent in the 2000.

The major multinational players in the organized sector of the industry are E Merck (India), Parke-Davis (India), Pfizer, Rhone-Poulenc (India), Glaxo-Wellcome, Novartis, and Smithkline Beecham Pharmaceuticals. The main Indian bulk drugs and formulations manufacturers in the organised sector are Dr. Reddy's Laboratories, Ipca laboratories, J B Chemicals & Pharmaceuticals, Nicholas Piramal India, Ranbaxy, Cipla, Sun Pharmaceuticals, and Wockhardt. The unorganized sector accounts for 30 percent of the total industry sales. Most of the players in

the unorganized sector are involved in formulations manufacturing, since this is not technology intensive.These players mainly cater to local demand and compete on price.

III. THE REGULATORY FRAMEWORK

Drug Price Control Order (DPCO)

DPCO was introduced in 1970 to ensure the abundant availability of essential drugs at reasonable prices through direct control over prices, with 22 drugs and their formulations being brought under price control. The DPCO was amended in 1979, 1987 and 1995, and the corresponding numbers of drugs put under price control were 347, 145 and 74 respectively. The minimum criterion for a drug to be included in the price control list under, under DPCO 1995, is that it should have an annual turnover of at least INR 40 million. A drug with a lower turnover can also be brought under price control if the drug has a turnover of more than INR 10 million and a single formulator has more than 90 percent of the market share. Similarly, a drug (irrespective of the turnover criteria) can be exempted from price control if there are at least five manufacturers supplying it.

Under DPCO 1995, for arriving at a price for a particular drug or formulation the government has defined a formula. The maximum sales price of a bulk drug is fixed by the government to yield a post tax return of 14 percent on the net worth or 22 percent on the capital employed. Manufacturers can choose any of these two parameters. In the case of a new plant, an internal rate of return of 12 percent on long term marginal costing may be allowed. In the case of imported bulk drugs, the landed cost (inclusive of import and customs duty) is the maximum permissible selling price. The government also determines the retail price for formulations (prepared from a bulk drug under price control). The rule allows the manufacturer to charge a markup of 100 percent as Maximum Allowable Post Manufacturing Expenses (MAPE) for scheduled formulations. MAPE includes all Costs incurred from the ex-factory stage to retailing including margins for the manufacturer and retailers. The pricing criteria for formulations is given by

Retail Price = (Material Cost + Conversion Cost + Packing material + Packing Cost) x (1+ MAPE) + Excise Duty

For imported formulations, the landed cost and the selling and distri-bution expenses, which would not exceed 50 percent of the landed price, form the basis of price.

Small-scale units were exempt from DPCO prior to 1995, but DPCO 1995 included small-scale units in its ambit. Moreover the DPCO also required pharmaceutical companies to maintain a ratio between the formu-lations and bulk drugs production, which was removed by the DPCO 1995.

DPCO has been successful in keeping drug prices among the lowest in India

but price regulations have mainly affected the MNCs as Indian companies got into manufacturing drugs, which don't fall under the purview of the DPCO. According to an estimate, 50 to 75 percent of their products are under price control, while Indian companies having nearly 15 to 30 percent of their products under price control. The reason being, while MNCs have always been formulations-driven with focus only on domestic market, Indian companies were primarily bulk drug producers engaged in exports. Only recently have they have started looking at the domestic market and for climbing up the value chain to enter the formulations business. This has led to restricted growth of MNCs in India and limited investment in the industry and has encouraged the growth of the Indian companies especially in the small-scale sector. Moreover rigid price with inadequate revision in accordance with cost increases have adversely affected the profitability of the manufacturers. Another impact of the DPCO on the industry has been the low R&D spending in India. R&D spending account for 1.5 percent of the turnover compared to the international level of 15 percent. The increased focus on exports, which are exempt from DPCO, decreasing import, tariffs under WTO obligations and rising competition among drugs under control have reduced the impact of the DPCO.

The Indian Patent Act (IPA)

The IPA (1970) — the regulation defining the protection to intellectual property — does not provide for product patents. Instead it allows for manufacturing processes to be patented. This has enabled the domestic pharmaceutical manufacturers to develop different processes and compete with international companies in the domestic markets. But India being a signatory to the GATT (now WTO) is obliged to ensure that IPA complies with TRIPS (Trade Related Intellectual Property Rights) agreement.

Intellectual property rights are the rights of the originator of an innovative idea or product to hold sole inter-national commercial rights over it for a period of time. Compliance with TRIPS would mean introducing product patents in India for pharmaceuticals for a uniform duration of 20 years for all products. India is entitled to a 10-year transitional period, making product patents applicable by January 1st 2005. However companies, which have filed patent applications from January 1st, 1995, will enjoy exclusive marketing rights. The impact of the prospective transition from the current process patent regime to a product patent regime in 2005 is likely to be felt only gradually over the next few years and in a substantive measure only after 2010. Till the new TRIPS compliant patent regime comes into force, Indian firms are free to manufacture drugs patented prior to January 1st, 1995. Moreover the patent laws will protect only a small proportion of drugs as the patented drugs form only 10 to 12 percent of the domestic drug turnover.

Another significant development is that many existing patented drugs will go off patent in next few years, opening up large generic markets for Indian manufacturers. The worldwide pharmaceutical market is worth USD 400 billion. Out of this about 70 percent comes from non-patented drugs. In the next five years with the expiry of several patents, the non-patented segment is expected to grow to 75 percent. This would also keep the drug prices from rising steeply. In the long run, new patent regime and introduction of new patented products, would encourage domestic companies to invest substantially in R&D to take advantage of the abundant pool of scientific and technical resources available here. Even MNCs have recognized the opportunities of cost effective R&D in India and are planning to outsource R&D to India. Few of the MNCs like Novartis A.G., Astra Zeneca plc, Pfizer Inc. and Merck Kga have already set up 100 percent subsidiaries in India to support new research activities. Another long-term strategy that can be adopted by Indian companies would be to manufacture cost effective intermediates for foreign companies. Joint Ventures, technology collaborations and cross licensing arrangements can also be examined.

IV. MAJOR SEGMENTS

Bulk Drugs

The field of bulk drugs is broad-based. It covers all products and preparations used in the production of pharmaceutical formulations. The bulk drugs industry segment in India has been able to establish its presence in the international markets and more than 60 percent of its produce is exported. This segment has managed treme-ndous growth, with production of only INR 0.18 billion in FY66, rising to INR 31.5 billion by FY99 and hence meeting 70 percent of the domestic requirement. The segment is a net foreign exchange earner producing export quality drugs, with bulk drugs export accounting for

60 percent of the total pharma industry exports. Exports of bulk drugs are growing by 30 percent year on year. But given the size of the world market, supply from India is miniscule - India's exports account for only 0.3 percent of the worldwide demand. In terms of the inputs used in production of drugs the industry faces low cost of inputs at competitive rates helped by the presence of a well-developed chemical industry.

As the manufacture of most bulk drugs is neither capital intensive nor technology intensive, process re-engineering encouraged the growth of production bases. There are a large number of bulk drug manufacturers in India, including many small-scale indus-tries. This has increased competition, leading to a drop in prices and consequently lower margins. Most bulk drugs under the DPCO sell below the government administered prices due to stiff competition and lower import tariffs.

Formulations

The size of the domestic formu-lations market is around INR 130 billion and it is growing at 10 percent per annum. India is largely self sufficient in case of formulations. Some life saving, new generation under-patent formu-lations continue to be imported, especially by MNCs, which then market them in India. More than 85 percent of the formulation production in the country is sold in the domestic market. Exports are largely to developing nations like China, South Africa, and CIS etc and to countries with weak patent laws. To access the generic (off-patent) formulation market of developed countries, Indian companies will need tie-ups with international majors. The number of varied formulations produced in the country has reached a staggering figure over the last decade. An esti-mated 15,000 formulations are manu-factured and marketed by the industry. Most of the formulation manufacturers have integrated backwards to con-solidate their position to improve their profitability. They have gone in for manufacturing of bulk drugs required as inputs for their formulations. The net profit margins achieved by the players operating in this industry have averaged around 5 percent over the last few years. MNC subsidiaries have over-taken Indian manufacturers by creating and selling branded formulations in the domestic market. In fact, they own 50 percent of India's top 20 branded formu-lations. The DPCO and IPA acted as effective deterrents. However the scenario could change once TRIPS formulated under WTO become operational in India.

V. SWOT ANALYSIS OF THE INDUSTRY

Strengths

- There is immense flexibility for the industry to move from one drug to another.
- Strong presence in the foreign markets, net exporter of bulk drugs & formulations.
- Advantage of low costs and availability of high skills in process development.
- Cost of R&D in India is much lower when compared to other nations.
- India has the third largest scientific pool in the world
- In volume terms, India consumes 8-10% of the world's volume

Weaknesses

- The industry is characterized by low margins.
- While India accounts for roughly a sixth of the world's population, it accounts for only a paltry 1.6% of the world's value of pharmaceutical consumption.
- This is a highly fragmented indus-try, with the top 10 players account-ing for 30% of the market share.
- The number of licensed manu-facturing units in India during 1999-2000 is around 23,790. Most of these units manufacture sub-standard drugs.

- R&D is an important aspect of the pharma industry, with the signing of WTO agreement; it is imperative for the Indian pharma industry to give greater emphasis to basic research for discovery and development of new drug molecules. Unfortunately R&D is a major drawback of the Indian pharma industry.
- The industry is plagued by price controls and inconsistent government policies.

Threats

- The pharmaceutical products are subject to high degree of technical obsolescence.
- WTO agreement would alter the pharmaceutical industry scenario drastically by 2005 AD. Most of the Indian companies do not have a research base. Such companies will be affected in the post WTO era.
- Exports of bulk drugs are vulnerable to the various changes in the international market.
- Small-scale sector will be severely affected in the time to come. They will be forced to close shop as manufacturing base for the bigger Indian companies or MNC's.
- China with its higher economies of scale can be a serious threat to the Indian industry.
- The chance of smaller players being taken over by larger players is high

Opportunities

- Many drugs are going off patent and the Indian pharmaceutical industry can take advantage of the situation.
- Pharmaceuticals and bulk drugs are identified as thrust areas for exports by the government. The government's attitude is positive towards the industry , which is evident from relaxation of products from DPCO.
- The latest trend in the industry seems to be towards a greater backward integration by manufacturing bulk intermediaries. This is a plus point to the industry since the intermediaries do not come under WTO agreement. This is one virgin area, which has not been tapped.
- Only 30% of the population has access to modern facilities.
- To create synergies through joining hand with other operators in the industry, go for backward and forward integration to utilize the resources in a better manner.
- India being a low cost producer of pharmaceutical products due to lower labor cost, R&D etc, the chance to strengthen presence in foreign market throws an important opportunity.
- The rising income level of the population in India concomitant with increased health awareness will result in an increase in the amount spent on health care.

V. BUILDING BRAND IN HEALTH SCIENCES: CHALLENGES

Brand and Healthcare

Quality is the essence of what it takes to "build brand" in the health sciences. Building an effective brand is a continuous process, and one that has been slow to gain momentum in the health care sector. While advertising can be used to increase awareness, advertising alone does not create a brand. A brand must be built by establishing quality at every level of the organization— from the front desk to patient care to the billing department.

My Brand Enhances My Assets

People consume more health products and services as they grow older, and building solid relationships secures customers for life.

Brand Defined

Quality is the essence of what it takes to reducing customer defections by as little as 5 percent can increase corporate profits by 25 percent to 85 percent. A strong brand increases market value, commanding 30 times its earnings at the time of a sale or merger, and institutional brand is a key tool in contract negotiations as well. Corporate brand can affect stock performances by 5 percent and one that has been slow to gain momentum.

Building Brand in Health Sciences Organisations

Instilling a brand in the minds of at target audience requires a clear understanding of how an organization is distinguished from its competitors. Core competencies—the characteristics that enable a company to create value for its customers—provide the competitive advantage on which its brand rests.

The Security Blanket: Integrity and Compliance

Building an ethical culture with effective communication is essential to earning consumer trust and confidence. This process must start with top-level management and incorporate continuous system-wide monitoring and improvement. Ethics-based compliance programs help establish corporate cultures that facilitate quality outcomes and a stronger brand. Compliance programs allow stakeholders to differentiate between organizations that are merely "getting by" and those dedicated to system-wide quality improvement.

VI. ALLIANCES: AN ANSWER?

Peter Drucker said thus:"The greatest change in the way business is being conducted is in the accelerating growth of relationships based not on ownership but on partnership."

Significant economic and socio-political forces are operating within most Western nations and their industries, leading to the adoption of alliance strategies. Careful selection of alliance forms and strategies can help firms within the pharmaceutical, biotechnology and medical technology sectors

to survive and thrive amid these powerful forces. Some of the most important drivers of alliances are the globalization of markets, growing international competition, and rising cost of bringing new products to market. Within the biotech and traditional pharmaceutical sectors these drivers can be grouped into four areas: stagnating R&D effectiveness; growing customer power and intervention; increasing globalization and competition; and increasing financial pressures. Alliances can play a role in responding to each of these challenges.

Why Should Firms Seek Alliances?

The three primary drivers are: the desire to share resources, to expand sales force coverage, and to access a product or process technology.

The motivations of smaller part-ners are illustrated by the case of T-Cell Science, a biotechnology company in Cambridge, Massachusetts. CEO Jim Grant has said that *"large companies need access to new technology,"* while the small companies need *"access to a number of things — especially money and markets."* Other, although somewhat less important, motivations include risk-sharing, accessing a foreign market, and reducing time-to-market. Motivations vary somewhat from country to country. American companies are primarily motivated by the desire to access a product or process technology, to share risk, and to access foreign markets.

The most important factor moti-vating Canadian companies to enter strategic alliances is the need to access a new sales force; the second-most- important factor is the need to share resources. Canadian companies use strategic alliances to penetrate new markets through alliances with well-established, indigenous companies.

Biotech companies are much more motivated by the desire to share risk and to access financial resources. An example of the latter is the establishment in 1996 of a minority equity alliance between Hemosol Inc., an emerging, well-financed, Toronto-based biotechnology company that is developing artificial blood products, and Fresenius, a leading German health care products company. The alliance provides Hemosol with support for licensing products in Europe, strong distribution capabilities in that market, and an alternate source of capital financing.

Alliances Can Add to Shareholder Value

Companies typically enter strategic alliances for the purpose of increasing shareholder value through profitable revenue growth and productivity improvement. They can achieve this goal by establishing one of several types of alliances. The correct choice depends on the specific objectives companies set for their partnerships. Such objectives may include raising capital, developing a new product or products, increasing economies of scale, co-branding, etc. By critically analyzing internal strengths and weaknesses, as

well as those of potential partners, strategic alliances can be structured to further shareholder value at different stages in the value chain. Indeed, proper internal and external diligence can provide the basis for creating a virtual corporation that enhances shareholder value. Strategic alliances to further shareholder value can be established at different stages in the value chain.

The different types of alliances include : research alliances, develop-ment alliances, sales and marketing alliances, manufacturing alliances, distribution alliances, and after-sales service alliances. This section describes the role of each type of alliance and provides illustrative examples of each.

Research

Research alliances have become more common over the last few years because of the increasing competitiveness in the market due, for example, to globalization. Many companies simply cannot rely only on their internal resources to generate the new ideas and innovations needed to facilitate and maintain company growth. As a result, they often seek alliances with smaller, more creative firms.

A portion of research expenditures can be recovered through tax deductions and research and experi-mentation tax credits. Tax credits are particularly attractive because they reduce tax liability dollar for dollar. Tax credits also improve earnings per share and enhance shareholder value. Thus, companies must be sensitive to the impact that such an alliance could have on the availability of such credits. Pharmaceutical companies also face a dilemma in determining which entity should fund the research and consequently own the resulting intangible assets. It is better to secure deductions and credits in entities in high-tax jurisdictions; whereas, it is beneficial to have the profits earned on intellectual assets in entities in low-tax jurisdictions. Careful thinking and planning must be done to implement solutions that achieve both objectives.

An example of such a mutually beneficial research alliance is AZA Research Pty Limited, a joint venture between Eli Lilly and Company and The Garvan Institute of Medical Research (a leading charitable biomedical research organization in Australia). Before entering this alliance, The Garvan Institute found that it could no longer rely on governments and private charitable organizations to fund its costly and high-risk early-stage dis-covery research. Therefore, the alliance with Eli Lilly was formed. The partner-ship gives AZA the right to sell Lilly's insulin and growth hormone products in Australia, and the proceeds of these sales are invested in endocrine research at Garvan. Eli Lilly, in turn, has the first option to market new products developed by AZA.

Product Development

The principal goal of some alliances is to accelerate the pace of high quality product/service develop-ment. Alliances can help companies to access

innovative product technology, and to incorporate new concepts in the final product design and avoid unforeseen difficulties that could lead to expensive and time-consuming redesign. Some companies also form alliances with firms that have comple-mentary development skills in order to create a superior or unique product.

Many pharmaceutical companies, for example, enter development alliances because of the increasing pressure from regulatory authorities to provide pharmacoeconomic and quality-of-life information. The pharma companies can achieve faster drug approvals by partnering with firms that are skilled in providing this information. Additionally, technology exchanged in alliances can be exploited for patent file extension for existing products through, for example, formulation or drug delivery improvement. Further-more, strategic alliances with firms that have established networks in offshore countries can help pharmaceutical companies gain approvals in those markets

Sales and Marketing

Traditionally, companies expand their sales forces by hiring more sales people. However, this approach brings with it the additional fixed costs of hiring, training, and managing new personnel. It also entails a long lead-time before an effective sales force is mobilized. Strategic alliances between firms with complementary sales forces can be a more cost-effective means of expanding sales coverage. Both partners can benefit by accessing more customers, increasing the intensity of their selling efforts to their clients, focusing on new clients, and driving sales in new geographic areas. For example, Metra Biosystems, a company that develops diagnostics for bone and joint diseases, formed an alliance with NovaDx to market the blood test Chondrex. This test measures the concentration of a protein that serves as a marker for arthritis and hence, can be used to determine the severity of a patient's disease and whether or not the patient is responding to therapy. By adding Chondrex to its portfolio, Metra Biosystems is enhancing its product line of bone disease tests. NovaDx, in turn, now has a partner in its selling efforts. Abbott Laboratories has also engaged in numerous marketing alliances with smaller firms. Abbott gains new products and its partnering firms benefit from the larger company's strong marketing resources. For example, Abbott has an agreement to market the diphtheria, tetanus, and whooping cough vaccines produced by North American Vaccine. North American Vaccine will receive a total of $42 million along with additional funds as the products are sold.

Another agreement formed with SONUS Pharmaceuticals will allow Abbott to market the contrast agent Echogen. This partnership provides Abbott with a more comprehensive product portfolio to present to physicians, and provides SONUS with payments and a share of the revenue for development and clinical support of Echogen.

Manufacturing

Typically, manufacturing alliances are formed to produce products more cost-effectively, as well as to reduce time-to-market. Smaller companies, in particular, can mitigate the financial risks associated with marketing new products by forming alliances with others that have expertise outside of their core competencies.

The manufacturer in such an alliance does not necessarily have to be the more efficient producer. A local producer, for example, may be able to avoid tariffs and duties, or may create savings in other parts of the supply chain (e.g., distribution costs). Chem-ferm, a partnership between Gist Brocades and DMS Andeno, is an example of a manufacturing alliance. The IPPD (Industrial Pharmaceutical Products Division) of Gist Brocades manufactures intermediates for the production of antibiotics. DMS Andeno specializes in the production of intermediate products for the pharmaceutical industry.

Faced with increasing competition from Asia and a consolidating client base, both companies decided that forward integration would be the best strategy for positioning their companies. Gist Brocades was skilled in the field of fermentation, while DMS Andeno was well versed in the field of fine chemistry. Therefore, by entering into an alliance, the companies were able to leverage their complementary stren-gths. In its first two years of operation, Chemferm exceeded its proposed financial objectives.

An Indian Example

Recently there has been a strategic business alliance between Wockhardt and Ranbaxy, two of the largest Pharmaceutical companies in India for the U.S market. This alliance will include Ranbaxy Laboratories (RLL) with its wholly owned subsidiary, Ranbaxy Pharmaceutical Inc (RPI), Princeton, New Jersey and Wockhardt Americas Inc, New York , the subsi-diary of Wockhardt, India.

The alliance is between the multi-product development prowess and manufacturing expertise and capacities of Wockhardt and the Sales and Marketing prowess of Ranbaxy to optimize the commercial value of these products and support a positive revenue stream for both the companies. This alliance is for Enalapril and ranitidine, two blockbusters now off patent.

VII. R & D : A TECHNOLOGICAL REVOLUTION

In the pharmaceutical industry's struggle to reach the levels of growth expected of it, one of its key aims will be to increase R&D productivity. And a key means of meeting this challenge is to adopt some of the new technologies and approaches broadly defined as genomics. That is bound to be a complicated, perilous, and often painful process, but if companies get their strategy right and overcome the obstacles, they could, in the best case, as much as halve the cost of drug development.

Impact of Genomics

As the science of genomics has advanced, so has the definition. When the term was coined in 1986, it referred mainly to the study of the mammalian genome—specifically, the mapping, sequencing, and analyzing of all its genes. The scope soon expanded, focusing not just on the genes' structure but on their function as well. More recently, the scope of the term has broadened further, focusing no longer just on knowledge of the genome but also on the exploitation of that knowledge, especially for health care.

Going beyond dictionary definitions, our interest is in what genomics means for the economics of pharmaceutical R&D. On the basis of our extensive research we suggest characterizing genomics, for the purposes of this study, as the confluence of two interdependent trends that are fundamentally changing the way R&D is conducted: industrialization (creating vastly higher throughputs, and hence a huge increase in data), and informatics (computerized techniques for managing and analyzing those data). The surge of data—generated by the former, and processed by the latter—is of a different order from the data yields of the pre-genomics era. To elaborate. The new high-tech industrialization has increased the efficiency of certain activities beyond recognition. Instead of assigning individual scientists to work manually on modest individual experiments, companies now invoke automation and parallel processing to conduct experiments much larger in scale and complexity, and at a much faster pace. The data that emerge are immensely greater both in quantity and in richness. Enormous databases—detailing gene expression, for example, or homologous genes across species, or protein structures— afford unprecedented comprehensive views of biological processes. Increasingly, researchers can understand properties of the system rather than just individual parts, and that holds out the promise of a more rational approach to drug discovery.

The new technology of informatics serves to handle and process all these data. Without it, the data would remain raw material. Informatics was nurtured by several coinciding factors: the ever-accelerating power of computers, refined algorithms, the integration of data and technology platforms, and the versatility of the Internet. The effect is that overwhelming masses of information can now be marshalled, managed, and analyzed as never before. Data are transformed into knowledge.

Opportunities

What is the impact of genomics on the economics of R&D? To what extent will genomics improve productivity overall, and what will its effects be when applied at various points of the value chain? What other incidental advantages might genomics bring in its wake? Realizing Savings Before genomics technology, deve-loping a new drug has cost companies on average $880 million, and has taken about 15 years from start to finish, that is, from target identi-

fication through regulatory approval Of this cost, about 75 percent can be attributed to failures along the way.

By applying genomics technology, companies could on average realize savings of nearly $300 million and two years per drug, largely as a result of efficiency gains. That represents a 35 percent cost and 15 percent time savings. (And those are the savings possible with technologies that are available today; when new or improved genomics technologies emerge, the savings will be even greater.) If companies wish to stay competitive, they have no choice: they must implement genomics technologies.

Diagram (1) shows the cost savings that occur by genomics and Diagram 2 shows the time saved.

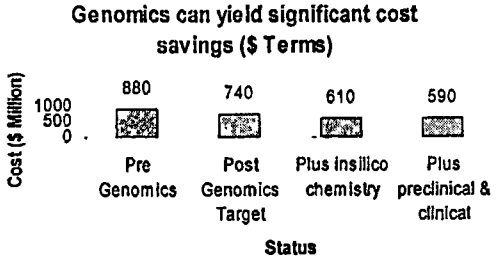


Diagram (1)

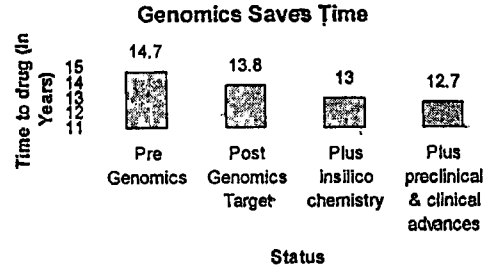


Diagram (2)

Doing so, however, will hardly produce such huge savings imme-diately, or automatically. It will take a few years, and many deft decisions, for the savings to be realized. The early years of implementation may in fact involve an increase in costs as the learning curve is negotiated for novel targets—specifically, as the necessary quality controls are established— and as major strategic decisions (about personnel and processes, for instance) are confirmed or revised. But first, we will take a closer look at the long-term upside, detailing the savings at various steps along the value chain.

The Challenges

Although implementing genomics offers companies great opportunities, it also presents them with formidable challenges. One of these is to ensure that the quality of the pipeline remains uncompromised. Another is to put the new technologies into efficient operation.

Maintaining Quality

If the potential productivity gains are to be fully realized, the post-genomics R&D pipeline will need to retain or improve its pre-genomics quality. Any decline in quality—the quality of targets and leads—would obviously have an adverse effect on productivity. The main threat to quality derives from the unorthodoxy, the unfamiliar nature, of so many new targets. Entire target classes, previously unknown, will need investigating. The temptation to pursue leads prematurely is bound to arise,

and quality control will need to be rigorously enforced to uphold the pipeline's usual success rates. To appreciate the threat accura-tely, we need a proper definition of the term quality. The "intrinsic quality" of a target or lead amounts to its likelihood of success, which is based on factors such as clinical relevance and drug ability. Companies can do little to alter this type of quality.

The "provisional quality" (or "informational quality") of a target or lead is based on the amount of data available on it at any given time—how much is known about its clinical relevance, drug ability, and so on. (This informational quality helps to predict success rates, but does not influence them.) Companies can alter this type of quality, by spending appropriately, and in that way can improve their ability to predict downstream success rates. This distinction is crucial. But it has at times been overlooked, resulting in some confusion in the industry. A widely publicized concern has been that novel targets identified through genomics would tend to be of inherently lower quality than pre-genomics targets, and thus more likely to fail at some costly phase downstream. That inference is an oversimplification, and is misleading. Certainly genomics proposes many more novel tar-gets (as much as 60 to 70 percent of potential tar-gets, in our interviewees' experience, may belong to previously unknown target classes), and their informational quality at that early stage is duly modest. But that says nothing about their intrinsic quality.

Any prudent company, no matter how bold, will strive to learn more about novel targets before deciding to pursue them downstream. In our analysis, investments made to raise a novel target's informational quality to the level of a known target's would be more than recouped in due course. The overall cost of these novel targets—raising their informational quality and then pursuing them down the value chain—is bound to rise initially. However, within three to five years from the initial discovery of a target in a novel class, according to our model, the overall cost increase per novel-class drug could return to average. Where do the added costs come from? And what must happen to offset them?

Cost of Quality Control

The typical increase will be about $200 million and more than one year per drug (that is, a total cost of $790 million versus $590 million, and a total time to drug of 13.8 years versus 12.7 years). The increase is mainly attri-butable to the extra time needed to understand target function and develop appropriate assays in target validation and screening; also, to the need to screen a higher proportion of compo-unds, since an appropriate subset of a larger library cannot be selected in advance. Chemical optimization costs would increase only if the novel target required a novel compound (by no means a necessary requirement, tho-ugh certainly a possible one occasio-nally). Our model examines this worst–case scenario explicitly. If a novel target does

happen to require a novel com-pound, or a compound unfamiliar to the medicinal chemists, the potential efficiency loss causes a further increase of $290 million and more than two years per drug (that is, a total cost of about $1.1 billion versus $590 million, and a total time to drug of 15 years versus 12.7 years). The additional increases here would be due to the extra time needed now for medicinal chemists to learn how to modify the compound and attain specific properties through trial and error. But this worst-case scenario should not be very common. Moving further still down the value chain, to the preclinical and clinical phases, costs are not expected to increase. The downstream success rate for novel compounds or targets should turn out to be much the same as that for known compounds or targets, as long as the same standards are applied. There should be no significant increase in toxicity or decrease in efficacy, other than in very unlikely circumstances—for instance, if existing animal models somehow proved less suitable, or if drugs for novel target classes were to interact with metabolic pathways in utterly unfamiliar ways.

Offsetting the Costs

Raising the informational quality of novel targets involves a heavy investment, but it is a wise investment. And a fairly quick one: knowledge about one novel target quickly elucidates other potential targets in the same class. Thanks to feedback loops, knowledge increases geometrically. As more is learned, the level of investment can tail off accordingly. In any case, the alternatives to making that early investment in informational quality are far from attractive. On the one hand, dropping the targets would be terribly shortsighted: companies would be forgoing the opportunity to discover and exploit untapped sources of revenue. On the other hand, pushing novel targets onward without adequate information on them would almost certainly result in a higher failure rate downstream, with all the associated implications for cost. An increased failure rate of just 10 percent across chemical optimization and all of development would on average increase costs by about $200 million per drug. To sum up, then: costs incurred early in the value chain (by information gathering) look preferable to those that would otherwise be incurred later (as the result of a higher downstream failure rate). All the more so, given that the early costs should soon begin falling (investment in information is almost always associated with an experience curve): as novel target classes become increasingly familiar, it will become increasingly efficient and economical to pursue new targets within those classes. So with proper handling, the burden of that early cost increase is just a short-term one, and the productivity of genomics-driven R&D should soon return almost to that of more familiar target classes. We estimate the time required for this is about three to five years from the discovery of a novel target, which is the amount of time it should take to complete validation and early screening (assay development).

Putting New Technology into Operation

It is one thing to acquire and install new capabilities and another to get them to function as they are meant to. The challenge of making genomics technologies operational has two major components: easing the bottlenecks that will develop, and resolving the personnel conundrums that are sure to arise.

Impact of Genetics

Having discussed the genomics wave, and the way that it promises to enhance R&D productivity, we now turn to the genetics wave. Several broad differences suggest themselves immediately. Where the genomics wave is technology-driven, the genetics wave is better viewed as data-driven, exploiting the known details of the human genome and individual variations within it. Where the genomics wave brings benefits mainly at the drug-discovery and preclinical phases, the genetics wave will prove its worth in both the earliest phase and the later phases of the value chain—target discovery and the clinic. Where the genomics wave enhances R&D productivity mainly by securing great improvements in efficiency (with only modest improvements, if any, in success rates), the genetics wave could boost success rates dramatically as well.

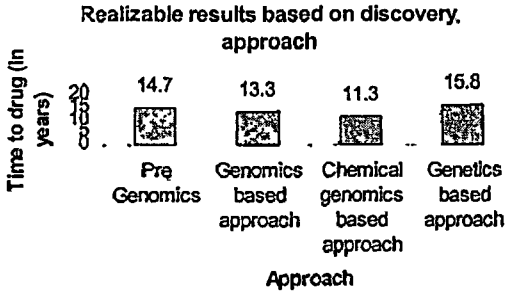
One further difference should be mentioned: where our model for the genomics wave was put for-ward with considerable confidence, our model for the genetics wave is more tentative. At this early stage, any assessment of genetics' impact on the economics of R&D is bound to be provisional. Certainly genetics has huge potential: if all goes according to plan, it will change R&D productivity beyond recognition. But between that potential and its full realization lie several years and many obstacles.

The potential consists in tremendous savings. First, genetics can bring about great efficiency gains by making it possible to shorten or even bypass various steps in the value chain. Second, genetics holds the prospect of transforming success rates: failures in the R&D pipeline currently account for 75 percent of the total cost of drug. But offsetting such opportunities, dangers loom large. Riding the genetics wave involves a greater risk than riding the genomics wave alone—though it is more exhilarating and, if the risks are successfully negotiated, ultimately more rewarding. How to choose between discretion and valor is a crucial strategic decision that companies will have to make in analyzing the economic implications of genetics, this chapter of the report considers the effect only on pharmaceutical R&D. But genetics is likely to affect health care far beyond R&D, in both the short and the long term. In the short term, new market opportunities should arise in the formerly sleepy diagnostics sector. (Drug companies may or may not be able to exploit these opportunities: In the longer term, genetics is likely to transform the delivery of health care.

Increasingly, diseases will be redefined into various subtypes—a refinement that should facilitate more appropriate care and more "rational" drug design. The combination of new diagnostics, new disease definitions, and new tailored drugs should prove a winning one, and may well usher in an era of individualized medicine. R&D remains the focus of our analysis here, however: specifically, the wide range of economic reactions that R&D might show under the impact of the new genetics information. We discuss the tremendous opportunities as well as the accompanying risks inherent in genetics-based R&D, and explore various ways of managing them.

Comparing Genomics and Genetics

Diagram (3) below shows the time saved using different approaches to drug discovery..



Managerial Challenges in R&D

The Story So Far

The genomics revolution is poised to sweep aside the old economics of pharmaceutical R&D. The biotechnology and pharmaceutical industries—and perhaps health care delivery in general—are on the brink of transformation, and companies that embrace the revolution in the right way stand to reap enormous benefits. Developing a new drug should become considerably less unpredictable and much less expensive. Companies will record improvements both in efficiency and in success rates all along the value chain, and the average cost and time needed to bring a new drug to market will fall correspondingly.

But this benign prospect is clouded by some warnings: great rewards will require comparably great efforts; a new paradigm in R&D economics may necessitate paradigm shifts in R&D management; above all, the great promise is offset by great risks—though, as in any revolution, the risks of standing aside may be greater than those of getting involved. Ensuring Your Future All biopharmaceutical companies are, or should be, actively deciding how best to engage in the revolution.

Making such decisions is no easy matter. The familiar bearings are no longer there, since the competitive and regulatory landscapes have changed so much—and continue to change—in response to the promise that genomics offers. Companies have been rushing to claim intellectual property rights (in the so-called IP land grab), now that the sequencing of the human genome has been completed. Statutes and court decisions regulating those IP rights keep emerging and modifying the

picture. And the corporate map is being re-drawn.

The major mergers of recent years have created industry superpowers, and the pace of acquisitions and alliances is set to quicken, if anything. With so much change occurring, there are bound to be winners and losers. Although the decisions will be unfamiliar and difficult, success will in the end be determined by traditional criteria. The winners will be those who make optimal strategic choices and then implement them in an optimal way. The two components of the winning combination will differ from company to company, according to each company's size, aspirations, financial power, capabilities, and so on. we identify the strategic and operational issues and examine the various options that different companies might exercise. To begin with the strategic issues, then—specifically, the challenge of defining a strategy in the genomics era.

Strategy : Searching for Genomic Competitive Advantage

Before genomics, biopharmaceu-tical companies used two basic tools—chemistry and molecular biology—to discover new drugs. Broadly speaking, the drugs that emerged were much indebted to serendipity. Research strategy consisted mainly of choosing which therapeutic areas to investigate, and discovery efforts focused on individual drug targets. Development provided even fewer strategic choices.

A promising compound emerging from chemistry would be tested on animals and humans in large and inefficient trials (inefficient because there was no means of identifying in advance likely responders or non responders). With the rise of genomics, there have come new technologies, new approaches, new information, and new ways of thinking about research and development. These have brought with them a new opportunity, or impera-tive, to turn research to competitive advantage. So companies now have weighty strategic issues to address. At the corporate level, the question is how much to invest, given the current environment. For R&D leadership, the question tends to be where to focus those investments—in what therapy areas, on what target classes, and so on—as well as which technologies to adopt and how to adopt them (in-house or externally, for example), and how to mitigate the associated risks.

Starting Position

Although these same broad questions will apply equally to all companies, there can be no standard answers. The actual options available to any company will depend on its starting position.

Company Size

A key constraint on a company's strategic options is size. The largest pharmaceutical companies boast capabilities and finances on a scale that allows full participation in the new technologies, even when the risk is high. Not that this exempts them from having to make choices. In fact, since

scale gives them so many options, they arguably carry a greater burden of strategic decision-making. How to select from such an embarrassment of riches? In addition, they face the challenge of managing complexity. If they are not selective enough, and embrace too many options, the operational problems could prove overwhelming. The narrower capabilities and lesser scale of small-to- medium-sized pharmaceutical companies and the larger biotech companies could represent either a severe drawback or a distinct advantage. On the one hand, there are reduced opportunities and even the prospect of being locked out by the big pharmaceutical firms: with disease genetics, for instance, a company with insufficient scale to build an in-house capability would risk forfeiting potentially lucrative intellectual property rights. On the other hand, since lesser scale often means lesser complexity, these modest-sized companies can compete more flexibly, changing their tactics quickly in response to technological advances or competitor moves. To see how scale can affect a company's options, consider the differing ways in which large and mid-size companies approach the target land grab. The larger companies have been able to take very aggressive approaches—scaling up or pursuing big deals to secure intellectual property rights to targets. The smaller companies, lacking in resources, have been unable to follow suit, but some of them have compensated by choosing very focused strategies, concentrating on their special competencies and imposing higher quality standards.

Building the Fact Base

Apart from company size, the two most important facets of a company's starting point are the beliefs and hypotheses held by its leadership team (roughly, its corporate culture) and its current R&D capabilities. Companies need to scrutinize both. It is crucial to understand and shape the beliefs and hypotheses of leaders throughout the organization, especially since, with genomics and genetics, the contributions and effects are cross-functional—that is, the managers or sections that contribute most are not necessarily those that benefit most. All those affected need to articulate their perceptions of the value and applicability of genomics and genetics to the company. Once tested, these perceptions should be given considerable weight when it comes to defining company strategy. An equally thorough assessment needs to be made of the company's relevant R&D capabilities—its technologies, skills, specific knowledge of diseases and disease mechanisms, and so on. Ideally, this will include an audit of current R&D productivity at every step in the value chain, identifying bottlenecks and other constraints. The more accurate and detailed the assessment, the more effectively the company can address the strategic questions as they pertain to its specific situation.

Corporate Decisions

How Much to Invest and Where?

As suggested above, even the largest pharmaceutical companies will have to make choices. Consider some of the huge deals of recent times: the $500 million deal between Bayer and Millennium for tar-gets, the $800 million deal between Novartis and Vertex for in silico chemistry, the $500 million deal between Roche and deCODE for disease genes. Note that these deals concern discrete steps of the value chain: in each case, it appears likely that the companies concerned were acting on an explicit preference—an established strategic preference. After all, given the magnitude of these deals, it seems unlikely that any one company would have placed all three bets. More to the point, such large deals, although essentially R&D ventures are not R&D decisions alone. Almost certainly, the decisions were thrashed out at the corporate level. For more modest-sized companies, strategic choices often go beyond matters of preference or emphasis. The question might be whether to concentrate all their efforts on some value chain steps and forgo others altogether. Certainly it no longer makes sense for even mid sized pharmaceutical companies to compete in target identification. And at the smaller end of the scale, companies with less than $400 million in R&D, say, may find themselves asking even more radical questions: Can we afford research at all? Should we not focus exclusively on licensing instead? Again, it is at the corporate level, rather than within R&D alone, that such questions will eventually be settled. It is not just through major partnerships and investment decisions, however that the corporate level is impinging on R&D strategy. More and more, specific R&D activities are having ramifications beyond R&D itself, and invoking corporate-level participation. Pharmacogenetics, for instance, often touches on corporate strategy as much as on R&D strategy. Should the company continue to pursue a promising compound, say, when the risk of market fragmentation might outweigh the positive market effects? Should the company attempt to resurrect candidate drugs previously killed because of rare side effects? And so on.

R&D Leadership Decisions: Where and How to Compete

With genomics and genetics now part of the landscape, R&D decision-making has become more complex. The options are far more numerous: there are more ways of gaining access to capabilities, more technologies to choose among, and even new dimensions in which to compete. R&D executives must select a combination of options that not only dovetail with the company's starting position and aspirations but can also be integrated smoothly with one another.

Choosing a Research Focus

The dimensions of competition include disease states. Some disease states have become more tractable,

thanks to genomics approaches, and any company continuing to investigate them will have to deploy genomics if it is to remain competitive. Just which therapeutic areas or disease states are most amenable to genomics is determined by several factors: the degree to which the disease is genetic in nature, the current understanding of disease processes at a molecular or genetic level, and so on.

They also include target class. Some genomics approaches are at odds with traditional therapeutic-area borders, and favor a broader deployment—around target class—rather than the old focus on disease state. (The targets within a class are usually similar in structure and bio-chemical function.)

Deciding How to Acquire or Gain Access to Capabilities

In general, there are several ways to attain a desired capability, but in some cases the options are limited. When the item is a proprietary database or tool, for instance, the company will have to license it in (or pay a provider for service) rather than buy it out-right; or when a company views its own information as too confidential to outsource, it will be forced to implement the related technology in-house. In many cases, though, a company will face the choice between building in-house capabilities and out-sourcing.

The in-house option, to justify itself, would have to confer some significant strategic or cost advantage. A company could have a cost advantage if it had developed a proprietary method, for example, or if it could boast greater scale or experience in a given approach.

Some though not all of the new technologies show clear scale benefits, thanks to industrialized processes and informatics. (Among the most obliging technologies in this regard are expression profiling, traditional HTS and μHTS, and exploitation of informatics-based analysis. The least obliging are medicinal chemistry and animal models, and some-where in between are compound synthesis and management, proteomics expression analysis, structural biology, and in silico chemistry.) Unfortunately, building scale in-house could be disproportionately costly for small-to-midsize pharmaceutical companies, even for the most scale-friendly technologies. These companies are unlikely to realize cost advantages; they risk spreading their technology dollars too thin. The wiser option would be partnering or licensing. If a company decides to develop a given technology in-house, it should review that decision regularly.

What is today a strategically advantageous capability may be commoditized tomorrow. The perception of sequencing, for instance, seems to be shifting, from a need-to-have technology to something that can readily be outsourced. If a company decides to outsource a given tech-nology, it will have to decide further on a prospective partner or partners. It might even opt to join forces with competitors. A model

partnership of this kind has been the SNP Consortium. A group of pharmaceutical companies, helped by various academic institutions, banded together to identify 300,000 SNPs (in the end, the total was about one million) and put them into the public domain. This joint effort had two very beneficial effects for its participants. First, it enabled the companies to concentrate more on their core interest, finding drugs; second, it forestalled the efforts of genomics companies, which would have sought to patent and extract rents from these SNPs. Other candidates for "competitions" of this kind include protein structure modeling and broad-scale sample collection for disease association studies.

Putting Strategy into Operation

Defining a genomics strategy is a good start, but even the most brilliant strategy is futile if it remains defined on paper 0only. The point is to put it into operation. Putting a strategy into operation consists essentially of making changes and managing them effectively. In the case of genomics and genetics, the changes that need to be made are profound, affecting all aspects of the R&D organization and, by extension, the corporation as a whole—core processes, organizational structure, job descriptions, interfaces, and so on. The necessary work can be divided into three broad areas: (a)Rebalancing the value chain; (b)Establishing the new organization and its governance; and (c) Managing organizational change

How Scientist's Job is Changing

R&D science is shifting from an arena of experimentation to one increasingly concerned with theoretical biology. The challenge is now less how to get the data than what to do with the data collected. Scientists who formerly could do their jobs virtually on their own—conduct their own experi-ments, and generate and analyze the data themselves—now find they need to collaborate with others who have more specialized technological skills, in areas such as informatics, robotics, or micro fabrication. Indeed, the scientists of the pre-genomics era are destined to evolve into two kinds of successors: those who interpret the data and devise plans for exploiting it, and those who continue to develop and optimize the technologies required for generating the data. (Companies should be sure to recognize and reward the latter group for its contributions, and not relegate it to second-class status.)

All scientists will need to become comfortable with new ways of working together—more sharing or collectivist now, less conducive to solitary initiative. The scientists of the future will still take responsibility for their own work, but perhaps will no longer take the credit for it: that will be ascribed to team effort.

Managing Transition

Changing from bench-based to information-based work in this way, and from favoring fairly independent endeavors to promoting a more collaborative ethos, is bound to be awkward or even

painful for most of those involved, scientists and managers alike. The formidable operational and organizational changes will entail cultural changes too: in fact, the new processes and structures may prove far less difficult to establish than new habits and attitudes. Consider informatics. It is not enough simply to introduce powerful new IT tools within traditional silos—within chemistry, for example, where in silico approaches would boost the efficiency of screening and optimization. To achieve their full impact, these IT tools need to be deployed across functions.

To bring biologists and chemists together, to incorporate data from the clinic into discovery, and so on. And that will require not just new software, or even new managerial positions, but new ways of thinking and of relating to colleagues. Some idea of what lies in store can be gleaned from the history of another transformational technology— CAD/CAM for airplane design. Like genomics, it promised to transform a costly and labor-intensive R&D process into a highly automated and efficient one. After languishing in niche applications in the 1970s and '80s, it finally proved its worth in the 1990s, when Boeing used it in designing the first "paperless" airplane, the Boeing 777. To exploit the technology fully, the company had to break down departmental barriers and encourage collaboration across the full range of functions. Jobs and job responsibilities had to change. Cherished traditions were called into question. The company held quarterly meetings at which employees could ask questions and voice their concerns. The transformation was a struggle, but ultimately a great success: Boeing continues to push the envelope in "in silico" airplane design. When pharmaceutical companies convert to genomics, they will have to temper the discomforts of transition in their turn. And that means engaging the emotional and behavioral issues—the human issues—as deeply as the operational ones.

Attentive management of the human issues, which has played such a prominent role in so many industries in the throes of reform, is going to be particularly crucial when it comes to the massive institutional changes demanded by the genomics revolution.

To stake a claim in the changing biopharmaceutical landscape, let alone feature prominently within it, a company will have to make itself radically amenable to change. Defining a strategy is certainly a step in that direction, and initiating that strategy is certainly a gesture of commitment. But wholehearted commitment is evidenced not by initiating the strategy but rather by maintaining it—that is, monitoring the new structures and procedures constantly, responding to shifts in external and internal circumstances, and introducing further changes repeatedly, aggressive or defensive, as new opportunities or new challenges arise, though always in line with the controlling wisdom of the strategy itself. If the unfamiliar outer landscape provokes feelings of unease, so too will a company's inner landscape, once all the requisite operational and organizational changes are in place. In particular, the in-crease in cross-functional activity may be disorienting for some executives of the old school.

Many of the ancient landmarks, tidy borders, and familiar categories will no longer be there to give them their bearings. Short of attempting a counterrevolution or withdrawing into obscurity, they will need to familiarize themselves with the new terrain fairly promptly—and accept it affirmatively, not grudgingly. Changes in attitude will perhaps prove the most difficult changes of all to bring about, and a company's prosperity could be in jeopardy if they fail to take effect.

The international pharmaceutical industry is pressing ahead in an unexpectedly difficult environment. Drug companies face unfamiliar frustrations. On one side, pricing policies are coming increasingly under threat (witness the recent moves in various U.S. states to restrict access to costlier drugs for Medicaid patients). From the other side, the pressure of expectation increases too, with financial analysts continuing to count on triumphant product launches and enormous growth. In such an environment, corporate well being, or even survival, depends on boosting productivity. It is against this background that the genomics revolution is unfolding. In their quest for improved productivity, companies should welcome the new technologies and approaches. Genomics promises prodigious benefits: it will unlock storehouses of information about the workings of human disease, and greatly refine—perhaps even personalize—health care. More to the point, it promises to trans-form how pharmaceutical research is conducted. The paradigm will shift from small-scale and serendipitous to global, industrialized, and systematic; and from methodical and compartmentalized to fluid and cross functional. The impact on R&D economics is likely to be tremendous: in the best case, productivity could as much as double. Looking beyond R&D, genomics and genetics also promise to transform the way pharmaceutical companies conduct their business in the coming years. If genetics realizes its potential, for example, treatments will become more sophisticated, markets may fragment, and the shape and value of marketing and sales organizations will change dramatically. The entire system of health care delivery, already in flux, will complete its metamorphosis. The offer that genomics and genetics are holding out is really an offer that companies cannot refuse. Companies that fail to accept the offer adequately will find themselves not simply uncompetitive but possibly right out of contention. There is nowhere to hide, and certainly no safety in inaction. To shun the promise of pharmacogenomics out of a fear of market fragmentation, for instance, is not to avert the fragmentation but simply to cede the market to one's rivals. Embracing the revolution appropriately will require both boldness and finesse: managers will have to make major strategic decisions, and to implement them will have to radically reconfigure operations.

The decisions take careful analysis to get right, and the operational hurdles need nimble negotiation to surmount. It all adds up to a formidable but by no means impossible task. And for companies that do it well, the rewards will be handsome. The opportunities are unprecedented. So are the challenges. The shrewd company will be one that remains responsive to both, as it tries to keep its head and to prosper in these revolutionary times.

VIII. BEST MARKETING PRACTICES FOR THE PHARMA COMPANIES

Advertising

- Substantial use of new electronic media
- Sophisticated targeting techniques to develop a more efficient media plan
- Extensive search on advertising copy effectiveness
- Sourcing techniques to decrease total cost of advertising
- Return on marketing investment

Promotion

- Return on marketing investments
- One to one relationship with customers
- Design of account specific promotional programs
- Design of geography specific promotional programs
- Use of extensive store data to design promotional plans

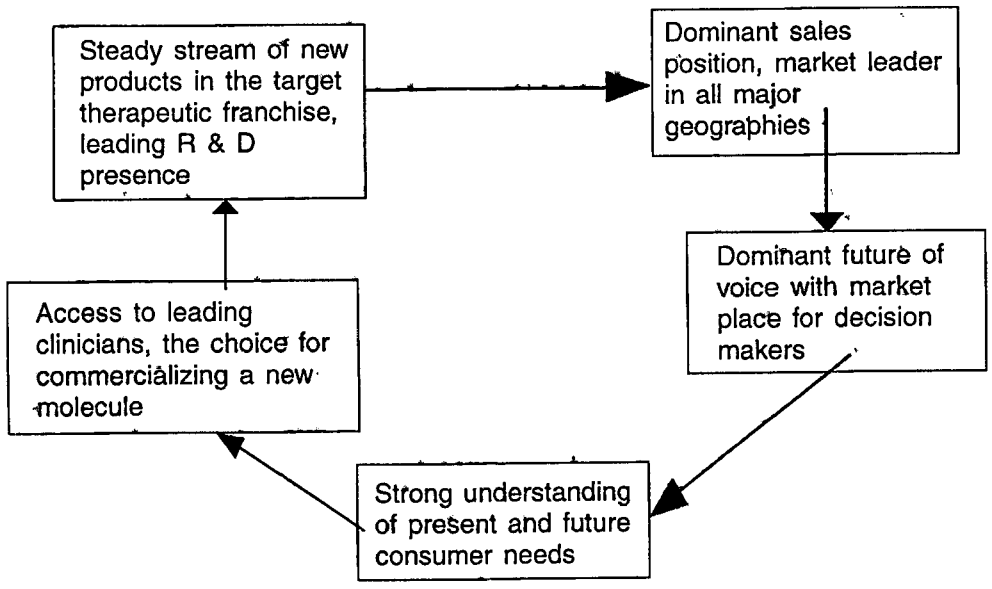
Brand

- Maximization of brand value through substantial brand extensions
- Use of sophisticated marker research techniques to select brand target segments and positioning
- Category management
- Creation of very strong competitive advantage by leveraging size/ economies of scale

New Product

- Short product development cycle
- Large number of new products introduced to preempt competition.

See Diagram (4) below on franchise management cycle.



Principles to Maximize Return on Marketing Investment

There are two aspects that need to be followed; they are elaborated as follows.

Optimized Allocation of Marketing Budget

- Product information
- Pharmacy promotion
- Sampling
- Symposia

Realization of Profitable Growth Opportunities

- Patient retention programs
- Post marketing studies
- Pricing models
- Other

Building Global Brand

To build blockbusters companies must start early, listen carefully, and spend wisely.

Blockbusters are not discovered, they are built. Current winners with the power hitting portfolios can attest the competitive advantages: ability to recruit and retain top talent, marketing economies of scale, greater access to medical thought leaders, a halo effect over smaller products in the sales rep bag and an enormous cash flow to fuel growth.

Now more than ever, pharma companies can literally add or subtract billions of dollars in the cash flow of a mega brands lifecycle R& D groups alone no longer drive the value of a new product. Sales and marketing teams, which have always had a role in a product's success, deserve a place at the head of the planning table.

Pharma companies spend $100 to $ 500 million to launch and market a blockbuster product so its annual sales must reach at least $500 million.

Top performers have developed rigorous resource allocation processes that enable them to identify early winners and prioritize accordingly.

There are five key drivers of success for blockbusters, they are explained in detail one by one.

Allocate Resources

No pharma product no matter impressive its profile can is destined to become a blockbuster without adequate marketing preparation and support. Research indicates that for current high potential products, companies spend an average $310 million and up to $500 million on marketing spanning the period from 5 years before launch to 3 years after. (That total excludes sales force expenditures) moreover, they invest more heavily in their high potential products rather than distributing resources evenly across the pipeline.

Although managers shouldn't welcome wasteful spending, they must give products with the greatest likeli-hood

of major commercial success adequate support for all marketing activities, including early and continuing market research, continuous thought leader development, speaker programs, journal publications, advisory boards, samples and supplies.

But more money is not the solution. Companies must allocate their spending wisely.

Companies must begin to invest earlier. Many therapies that appear promising in the clinic perform disappointingly in the market. One key factor in such disappointments is inadequate marketing support during early product development.

Close analysis of leading firms reveals that rapid sales uptake is a consequence of cumulative marketing investment over several years rather than extravagant spending just before or during launch. Average marketing spend during early stages is relatively low. But during that phase, marketing staffs conduct crucial market research that helps identify unmet medical needs, market opportunities and competitive issues- key components that drive early market assessment and product profile development. Such early development helps shape clinical trials, ensuring their alignment with unmet medical needs and marketing requirements. Without such market driven shaping products reach the poorly positioned to meet current medical needs as defined by practicing doctors.

Market Focussed R&D

Successful firms work hard to break down the walls that have traditionally separated R & D and marketing. Research scientists now co ordinate their efforts as early as the pre clinical phase. Such co ordination helps shape product candidates and aligns them with unmet medical needs, new market opportunities and competitive positioning. Marketing personnel are keen on building market share and influencing key customers and thought leaders, while clinical people tend to focus on the efficiency of clinical trials and bringing the product to the market as soon as possible. Aligning these two sets of goals is critical to effective partnership.

Part of the integration process is to co ordinate cross functional teams, structures and processes to optimize a new product's position .No longer is it enough to be first to market. Industry annals document more than a few cases of first o market flubs. The new mantra is to speed market penetration, which implies both development speed and market needs alignment. Many factors contribute to a culture of support for market-focused development. They are:

- Management support
- Incentive links
- Performance management links
- Team and skill training
- Communication support

- Relationship orientation
- Structural alignment
- Thought leader guidance
- Process focus
- Co location of key team members
- Rapid knowledge sharing
- Technology enablement

The firms are intensively self-critical of their efforts to integrate R& D and marketing.

Thought Leader Management

Within the product development process, thought leaders are like a compass pointing to the true north, providing invaluable insight into unmet medical needs, competitive dynamics and the future direction of therapeutic care. In view if the multi year cycle of drug discovery, development and launch, its nearly impossible to create new products that reflect customer needs without consistently viewing the marketplace through the eyes of thought leaders from diverse segments of the pharmaceutical and healthcare industries.

Consequently, firms have to focus on the quality of their thought leader management programs. Winning practices drawn from the majors firms include:

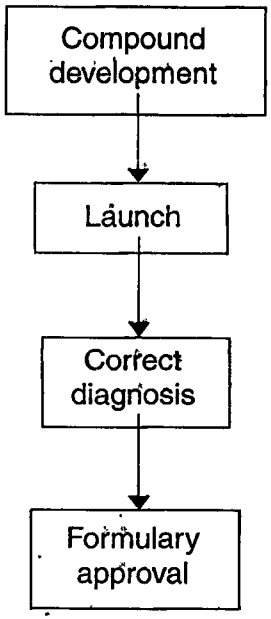
- Target and employ a cross section of thought leaders to balance medical perspectives with commercial interests
- Develop a systematic process to build long term relationships with thought leaders in strategic therapeutic areas
- Develop relationships with top global thought leaders to shape the design of Phase I and Phase II clinical trials
- Involve regional and Non US affiliate level thought leaders in the execution of phase III clinical trials
- Manage advisory boards and local thought management leader speakers to enhance product acceptance
- Establish global advisory panels to obtain early inputs from country units on clinical development and marketing plans

Thought Leader Relationships

Best in class companies manage thought leaders through formal structures, value added programs and integrated services:

- Formalize key personnel roles and responsibilities
- Provide crucial insight for market focused development
- Develop insight for growth
- Develop insight for product position and launch
- Block competitors from accessing same insights with relationship management

The flow chart below explains the track to be continuously observed by the thought leaders to try and ensure success.



Broad Based Market Research

Market research has always been a cornerstone of market sizing and product development. Now its becoming necessary to ensure that clinical development is anchored in market needs.

Top firms conduct a wide spectrum of market research from pre clinical to post launch phases, providing critical data and insights that drive decisions ranging from the target profile to clinical trial design to competitive positioning to branding and phase IV studies.

The following is the market research model .The key is to conduct early and continuing market research to drive product development and market positioning.

Pre Clinical

- Therapeutic opportunities assessment
- Competitive assessment
- Focus group with thought leaders
- Initial pricing studies
- Pre efficacy forecasting

Phase I

- Success factor analysis
- Attribute mapping studies
- Conjoint analysis
- Global forecasting model development
- Global payer and value pricing study
- Health economics research

Phase II

- Market situation needs analysis
- Initial quantitative product profile with pricing study
- Post efficacy forecast for product decision
- Conjoint global analysis
- Patient segmentation attribute mapping and physician segmentation
- Trademark development

Phase III

- Positioning study
- Package design study
- Brand name study
- Branding test
- Line extension study
- Life cycle contract
- Pricing and reimbursement
- Final positioning check
- DTC message development
- Position message development
- Concept development testing

Submission

- Definitive pricing study
- Reforecast
- Market attitude & acceptance study
- Competitive analysis
- Journal ad recall test
- Promotional piece development and testing
- Managed care study
- Pharmacist research
- Long term care research

Launch

- Launch and post launch tracking
- Promotional ROI analysis
- Message recall and promo refinement
- DTC monitoring
- Post launch positioning and repositioning studies
- Research for new indications

Sales Force Support

Sales force support has to be given high weight age. At the end of the day if the sales organization does not enthusiastically embrace a new product the product will not achieve optimum market potential. For a successful product launch-especially of a potential blockbuster- the company must inform and involve the sales force early. There is a direct relationship between the comprehensiveness of information at the reps disposal and their ability to sell a new product enthusiastically and effectively. It is important that the reps undergo extensive training before beginning the promotional activities. To achieve this it is vital to implement a care fully orchestrated set of activities in the 12-18 months before launch. All actions ranging from product potential communications to sales incentives plan specifics – are designed to stimulate sales representatives, prelaunch product awareness, education, excitement and commitment.

IX. CONCLUSION

There might never be a foolproof method but the answers have been found to most of the questions initially posed. They are elaborated as follows:

- Can the Indian firms raise sufficient finances from the market? Do they need to enter into tie-ups with MNC's? The answers can be found in the solutions provided by alliances.
- Where is the industry today, what are its strengths and weaknesses, do we possess the scientific talent? The answers can be found in the overview and the thoughts on the Indian pharmaceutical industry that clearly illustrate the highly fragmented Indian industry, its low cost of manufacturing, weaknesses in fundamental product research and its reverse engineering capabilities developed as a result of government policy. The vast scientific talent pool is there to be optimally utilized, as new policy and commitment to integrate with the global economy would eventually force us to harness the abilities of the very best that we possess.
- What will be the technology of the future? The project places tremendous emphasis on the significant role of technology and the way it needs to be viewed i.e. to find new ways to discover a drug or to cut costs and save time or both. The answers are provided by both genomics and pharmacogenetics coupled with information technology.
- Do the marketing fundamentals remain the same, how to identify the blockbuster therapeutic category? The integration of various functional activities of pharmaceutical firms with marketing highlights the new paradigm that is beginning to appear. The involvement of thought leaders would provide the answer to the critical question of correctly identifying the blockbuster therapeutic category.

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