CHAPTER - 4
PRICES AND POLICIES

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Chapter 4

PRICE, POLICIES AND REGULATIONS

4.1 Introduction

This chapter draws our attention towards determining the drug prices, policies and regulations and its impact on Indian pharma companies. In second section, Pharma revolution in the global prices, determining drug prices and measure of the drug price are discussed. The policies and regulation and the legal regulatory environment has been discussed in third and fourth sections. It also highlights government policies and drug control order in India.

The drug and pharmaceutical industry in the country today faces new challenges on account of liberalization of the Indian economy, the globalization of the world economy and on account of new obligations undertaken by India under the WTO Agreements. These challenges require a change in emphasis in the current pharmaceutical policy and the need for new initiatives beyond those enumerated in the Drug Policy 1986, as modified in 1994, so that policy inputs are directed more towards promoting accelerated growth of the pharmaceutical industry and towards making it more internationally competitive. The process of liberalization set in motion in 1991 has considerably reduced the scope of industrial licensing and demolished many non-tariff barriers to imports. (Schweitzer O.Stuart, 2007)
4.2. Pharmaceutical Revolution /Global Prices

The issue of drug prices has led to policy debate for 40 years with conflicting arguments that the industry is making above average profits based on monopolistic structure. As in the first hearing over 40 years ago, the major issue was price inflation of pharmaceutical. But the pharmaceutical industry replied to the contrary that prices were low relative to the value affordable to consumer, and high returns on successful products were required to balance the losses from the large number of unsuccessful ones. They argued that if drug prices were to be judged against marginal cost as price determination under perfect competition would suggest, then marginal cost must be defined to include the cost of developing and marketing new products. If marginal cost were defined this way, prices would not be seen as excessive at all. Although it admitted earning substantial profits, the industry argued that without these returns, research outlays would be limited and the number of new drug reduced. (Schweitzer O. Stuart, 2007)

4.2.1. Determining the Drug Prices

Underlying the debate over drug prices is whether they are set primarily by supply-side factor as cost or by demand factors such as drug attributes. The former would suggest monopoly power of the industry. In a competitive market, price is determined jointly by demand and marginal not total cost. It is unexpected to hear industry representative concur with their critics that costs especially of R and D determines prices as could occur in monopolistic or imperfectly competitive market. It can be seen demand and especially product characteristics, have a far greater role in pharmaceutical prices determination than has been acknowledged, even by the industry itself. (Barnett CL, 1979)
Economic theory suggests that in perfect competitive market a consumer’s demand curve for a particular good / services is perfectly elastic, with even small price increase leading the consumer to shift purchases completely to competing products. Perfect competitive markets are rare but do occur among commodity such as agricultural product, natural resources and computer memory chips. For producers to sell products in such market, prices will be bid down by producers to the point MC=Price is the product’s price and marginal cost is marginal cost of producing the products by the most efficient firm price will be so low that any successive price reduction will cause all the producers to shut down. The prices however include normal profit for the producer, equal to the rate of return on its investment and its own labour that it would earn in the next most profitable industry. (Boughton B, 1996)

But whether pharmaceutical industry is perfect competition it may be argued that it is for some products, such as generic penicillin, where many firms produce the product and brand loyalty is slight. But product differentiation exists for most pharmaceutical, even when they compete with one another. Product differentiation and brand loyalty suggest that consumer demand is not perfectly elastic, but is downward sloping. When a firm produces at level of output where MC=MR, price will be above the intersection of the MR and MC curves because demand curve the firm is facing downward sloping in the fig
Hence price is determined jointly by the shape and position of the MC curve as well as the shape and position of the demand curve. Prices can’t be set by either supply and demand factors alone. Manufacturing costs are low in this industry. In fact the pharmaceutical industry is less like other manufacturing industries and more like the computer software or movie industries in this regard. It even resembles infrastructure investment such as roads, bridges with high fixed cost and low marginal cost. The additional cost associated with producing an additional unit of output is very small in all of these industries. (Browning E and Browning J, 1993)

Both research and marketing costs in the pharmaceutical industry however are usually incurred before the final products are manufactured and so they don’t change with the volume of production. Hence they are termed fixed or ‘sunk cost’ MC determines price in a competitive market, but fixed cost don’t. The industry’s position has
consistently been that these costs must be covered by price of the final product. If these fixed costs are not covered, the firm will lose incentive to develop and promote more innovative drugs.

Firstly it is argued by the pharmaceutical industry and its critics, R and D investment is predetermined. The costs of this investment determine the total cost which with profit goals determines price. Prices determine quantity demanded and ultimately profit. Prices are set according to cost. This model assumes that investment is predetermined and that cost determines prices.

FIG 4.2: A COST DRIVEN MODEL OF PHARMACEUTICAL PRICES

An alternative model shows product attributes as a demand variable determining price. In this model price is determined by drug attributes not costs and profit determine future investment. Prices if new pharmaceutical vary according to their degree of innovativeness. Major therapeutic advance, are able to command a substantially higher prices differential than that of drugs offering only a modest therapeutic advance. Drugs embodying only modest improvement still allow firms to charge somewhat more than existing drugs. But drugs offering little or no therapeutic advance are unable to charge more than existing drugs. (Clarkson K, 1993)

Next is a price change after launch. There are two pricing strategies consistent with the Lu and Comanor findings. One is penetrating strategy in which a drug is initially priced low price to gain market share , then the price is raised overtime .In contrast other drugs are launched at a high price and Price increases are small overtime. This skimming strategy was followed by innovative drugs while the drugs with limited therapeutic gain followed the penetration strategy undercutting competitors to take
away market share and then raise prices once brand loyalty was established. (Comanor WS, 1986) There is direct relationship between therapeutic improvement of new products and their launch and subsequent prices. Prices of innovative drugs are different from those of the previous products which are less innovative both at launch and later. In other words, price is related to the quality of a drug.

Third observation support the importance of consumer demand on price is the widespread existence of price discrimination in the pharmaceutical market. Price discrimination occurs when the same commodity is sold at different prices to different consumers. There is evidence that this pattern has occurred in the pharmaceutical industry, it had in other consumer goods market such as telephone charges and airlines fares. (Comanor WS and Schweitzer SO, 1994) Firms want to price discriminate among classes of consumers because profits rise when price is set according to each consumer group willingness to pay, as measured by respective demand schedule. We expect to find different prices charged to different buyers where the prices depend on the demand conditions and also where there are clear distinctions among types of buyers.

The theory of price discrimination suggests that prices will depend primarily on relevant price elasticities of demand of the various consumers. Whenever these elasticities differ among classes of consumers, prices are likely to be different. In the past wholesale prices paid were typically lower than those paid by retail pharmacy. Consumers with high demand elasticity, especially managed care programs paid lower prices than did purchasers who are less price sensitive, such as retail pharmacies. Demand by hospitals and other major purchasers for specific products is
likely to be elastic because they can decide a priori which products their physicians will use. (Schweitzer O. Stuart, 2007)

Individual pharmacies by contrast must stock a large number of products to fill individual prescriptions. Their role is much more passive in terms of product selection. Differences in demand elasticities are reflected in differences in actual transaction prices at the wholesale level. These discounts may also differ between individual and chain store pharmacies and between hospitals and Health Maintenance Organization (HMOs). A critical fact about the pharmaceutical industry is that there is no single price for an individual product, even at specific point in time prices depend on demand conditions presented by particular buyers.

When generic products enter the marketplace, they typically appeal more to some buyers than to others. E.g. HMOs and hospitals are more likely to use generic products because they have the knowledge and expertise required to evaluate them, in contrast to individual physicians. One therefore expects that generic rival will make greater sales inroads to some buyers than to others. So producer of innovative products will respond to generic competition more strongly in some market segments than in others. By setting much lower prices where generic competition exists and keeping price at their original level or even higher where generic competition is less important, the original sellers of many products have been able to maintain a large proportion of their original sales revenue even after patent expiration. (IMS Health, 2004)

So skimming and penetration pricing behavior together with price discrimination are characteristics behavior for pharmaceutical and reflects the relationship between the demand condition and price in the drug market.
4.2.2 Drug Prices Vary across Country

According to Stuart O. Schweitzer, 2007 in his book the drug prices are expected to vary internationally because of differences in demand conditions in various countries. The first determinant of the price people in a country will be willing to pay for drugs is the country's income. The quantity of pharmaceuticals (and everything else) that people are willing to purchase typically rises with the level of income. The amount by which the quantity demanded rises with income is defined as the income elasticity. Thus the demand curve for people in a wealthy country will be to the right of the demand curve for people in a poor country.

FIGURE 4.4: DEMAND FOR PHARMACEUTICAL VARIES

Demand curves D1 and D2 describe the relationship between price and quantity demanded for drugs in two countries: a wealthy country, with demand curve D1, and a poor country, with demand curve D2. Each of the demand curves is associated with a marginal revenue (MR) curve, MR1 and MR2, showing the addition to total revenue as additional units of output are sold. The downward slope of the demand curve tells us
that as one more unit is sold the addition to revenue is not merely the price of the last unit but must reflect that all units have to be sold at this new (lower) price. Marginal revenue is therefore lower than the demand curve at any price. (Morrison S, 1993)

If a pharmaceutical manufacturer produces its product with marginal costs described by curve MC, it will maximize profits by producing at the level of output such that $MC = MR$ for each market. MC intersects the respective countries' marginal revenue curves $MR_1$ and $MR_2$ at points 1 and 2, respectively. The price paid by consumers in the wealthy country will be $P_1$ for quantity $q_1$. Consumers in the poor country will pay price $P_2$ for quantity $q_2$, with $P_1 > P_2$.

This is one explanation for drug prices being lower in poor countries such as Mexico and China than in wealthy countries such as the United States and Switzerland. The same relationship will hold for virtually all consumer goods including housing, food, and clothing, as long as the location of the demand curve is at least partly determined by income. (Pharmaceutical Research and Manufacturers of America, 2002)

But there is a second reason why prices vary across markets, and this deals not with the location of respective demand curves but with their shape, or, more precisely, the respective price sensitivity, or elasticity of demand. This relation is called the theory of price discrimination and is based on the profit-maximizing firm's desire to charge each consumer what he or she is willing to pay, and not merely what the last consumer pays. (Reekie WD, 1976)

The demand curve shows the price that will lead consumers to purchase a particular quantity. Normally, this implies that all consumers pay the same price—the price paid by the person buying the last unit of the good or service depicted by the demand curve. But some consumers are willing to pay a higher price than the price of that last
unit. And typically all consumers are willing to pay a higher price for a smaller quantity, with an increasingly lower price for successive units.

If different consumers are charged different amounts it is imperative that the various buyers not be able to bargain among themselves. The price discrimination occurs whenever a producer is able to sell the same product to a different group of buyers, each with different demand elasticity. (Perloff J, 1995)

In the case of Pharmaceuticals, patients in wealthy countries will tend to be less price sensitive in their demand for pharmaceuticals. This results in part from people's preferences for medical care to maintain their quality of life, and in part from patients in wealthy countries being more likely to have insurance coverage to shield them from the full cost of drugs. Insurance coverage tends to lower consumer demand elasticity. For both reasons, patients in wealthy countries will have lower price sensitivity to drugs, being less willing to substitute less expensive drugs for more expensive drugs, and also less willing to forego use of drugs, than patients in poorer countries. We see, therefore, that both the position of the demand curve for pharmaceuticals and its shape (elasticity) will lead to higher prices for drugs in wealthy countries than in poor countries. (Morrison S, 1993)

4.2.3 Measure of Drug Prices across Countries

In choosing drugs to be compared, products should be identical in at least two of the following three characteristics: chemical composition, brand name, or manufacturer. This matching will include some unbranded generics, and is therefore broader than the same-manufacturer requirement used in other studies, but still excludes branded generics and originator products licensed to other manufacturers and sold under
different names. Alternatively, one could match products on the basis of molecule/therapeutic category (MOL/ATC), comparing the weighted average price over all products with the same chemical composition in the same therapeutic category, regardless of manufacturer or brand.

Second, if one wants to compare the effect of price differentials on consumers, prices should be compared at the retail level, rather than at the ex-manufacturer level. The difference between these two prices is the mark-up, or distribution margin, which includes the profits of both the dispensing pharmacy as well as the wholesaler if one is involved in distributing the product. In many discussions of the cost of Pharmaceuticals, there is the implicit assumption that distribution margins are constant across products, with retail prices comprised of the wholesale price plus a fixed amount added to cover distribution costs. However, that picture is not accurate for the U.S. economy. (Steiner, 1993) has pointed to the "inverse association between the margins of manufacturers and [those of] retailers." Salehi and Schweitzer (1985) found that the relationship also applies to Pharmaceuticals. Branded Pharmaceuticals, which typically embody a high manufacturing margin, have lower distribution margins than those of generic products, which have relatively low margins at the manufacturing stage and higher distribution margins. (Schweitzer O.Stuart, 2007)

As a result, price differences between branded and generic products are greater at the manufacturing stage than they are at the retail stage. Manufacturer prices are therefore poor proxies for retail prices. In addition, wholesale or list prices are not indicators of transaction prices of prevailing discounts and rebates, especially in the United States. Moreover, prices should refer to the most popular package size for a drug, not the package size that manufacturers provide to wholesalers or retailers. These large
manufacturer packages will be broken up when they are distributed to consumers, and the prices are likely to overstate retail package prices. Finally, both exchange rates and purchasing power parities (PPP) should be used to convert local prices to a common currency. PPP is an attempt to adjust official exchange rates for the average price level in different countries.

The methodology of a study by Danzon and Chao (2000) is largely consistent with the above criteria, and corrects for many of the deficiencies various studies. The study compares prices in seven countries for Intercontinental Medical Systems (IMS) data for all outpatient drug sales in 1992. Danzon and Chao (2000) found that price differences between countries depend greatly on the way in which the comparison is framed, particularly, which country's quantity weights are used to construct the price index. Comparisons also differ depending on whether one compares prices per gram of active ingredient or prices per "standard unit" (e.g., per capsule or milliliter of liquid).

The Laspeyres indexes for price per standard unit (SU) show smaller price differences than those reported in other studies: Canada and Germany, respectively, are 2.1% and 24.7% higher than the United States; Japan, Italy, and the United Kingdom are, respectively, 11.6%, 12.9%, and 16.6% lower than the United States; and France is 32.2% lower than the United States. (Landers P, 2003)

With the Paasche indexes, all countries appear to have lower prices than the United States, ranging from 44% lower for the United Kingdom to 67% lower for France. Thus, both the magnitude and rank ordering of price differentials depend on the weights. For given weights the standard unit (SU) and kg [gram] indexes differ significantly for some countries, due to systematic differences in grams per standard
unit SU. Strength per dose in Japan, for example, is typically weak, in part because doctors commonly prescribe several drugs to be taken together (polypharmacy). Japan thus appears 11.6% less expensive than the United States on the basis of price per standard unit SU, but 19.3% more expensive on the basis of price per kg, because more pills are required to yield a given total gram (Danzon and Chao, 2000).

These results indicate that differences in mix of products, dosage forms and strengths, and pharmacy type contribute significantly to the measure of price differences. Danzon and Chao conclude the following:

Quasi-hedonic regression shows that cross-national price differences reflect differences in product characteristics and in their implicit prices, which reflect the regulatory regime. Strict price regulation systematically lowers prices for older molecules and globally diffused molecules. Generic competition lowers prices in less-regulated regimes, which also have more price-elastic demand. (Danzon and Kim, 1993)

4.2.4 Why Drug Price Differences Persist

The first consideration in explaining international drug price differences is differences in tastes and preferences that alter demand. Significant differences exist across cultures, for example, in choice of drugs as well as their dosage and form of administration (Payer 1988). Another important consideration is the physicians' economic incentive in determining drug demand and price. For example, in Japan, physicians tend to prescribe heavily at each office visit, because of the high "doctor margin" in the health system that supplements reimbursed fees. This margin is the difference between official drug prices, set by Japan's Ministry of Health and Welfare,
and the discounted price at which drug wholesalers sell their products to hospitals and doctors. U.S. physicians, for the most part, do not have such an incentive, and in the United States, drugs only account for about 10% of health spending, whereas in Japan, nearly 17% of the total health care bill is spent on Pharmaceuticals.

Government regulation and third-party involvement also influence drug price and consumption volume. Governments in many other countries regulate prices either directly or indirectly, as described by (Danzon and Kim, 1993).

France and Italy directly regulate prices at launch and the subsequent rate of price increase. Germany, the Netherlands, Denmark and New Zealand operate reference price systems of reimbursement and thereby exert strong pressure on prices charged by manufacturers. The UK operates a system of profit regulation that constrains prices to yield no more than a target overall rate of return on capital in the UK. The Canadian government monitors price levels at launch and rates of increase to assure that they are "reasonable." (Schweitzer O. Stuart, 2007)

4.3. Policies and Regulations

Statutory controls on the prices of drugs were imposed for the first time in India in 1962 in the wake of Chinese aggression and declaration of emergency. The Drugs Price Order, 1962 issued mainly to contain the inflationary forces expected as a consequence of the war required the manufacturers, importers and distributors of drugs to publish price lists of their products and chemist dispensing them to display such price lists on their premises. The Drugs Price Control Order- 1963 was promulgated freezing the sale prices of drugs at the level of obtaining on first April
Both these orders were issued under the defense of India Act. (Chaganti Subba Rao, 2007)

TABLE 4.1 PRICE INCREASE DURING 1967-69

<table>
<thead>
<tr>
<th>Order of price increase</th>
<th>Number of formulation</th>
</tr>
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<tbody>
<tr>
<td>Below 10</td>
<td>124</td>
</tr>
<tr>
<td>10-19</td>
<td>205</td>
</tr>
<tr>
<td>20-29</td>
<td>107</td>
</tr>
<tr>
<td>30-39</td>
<td>41</td>
</tr>
<tr>
<td>40 and above</td>
<td>44</td>
</tr>
<tr>
<td>total</td>
<td>521</td>
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The range of price increase allowed during November 1967 and December 1969 on 521 applications received for price revision.

Since 1966 the government has periodically set up tariff commissions at an interval of three to seven years to look into the control of prices and related matters of pharmaceutical products. The inferences of various tariff commissions till 1973 are as follows:
1. The prices of selected bulk drug were much lower in most cases in other countries and the prices of formulations in the Indian market compared favorably with prevailing prices of similar formulations in other countries.

2. The major factors responsible for high prices of bulk drugs as compared to developed countries were due to high cost of equipments intermediaries and raw-materials a major part of which was imported.

3. Fix the prices of drugs on the basis of a rational formula that could be applied uniformly to all formulations and products.

4. Provide adequate incentives to the industry to continue the growth from the basic stage and develop research and development facilities and provide more employment.

5. During the later part of 1973 the prices of petrochemical based materials increased considerably due to oil price hike by OPEC countries. These form significant proportion of pharmaceutical raw materials and resulted in further escalation of manufacturing cost. There was a general decline in the ratio of profitability on sales from about 15.5% in 1969-70 (pre DPCO year) to about 8.4% in 1972-73 (Chaganti Subba Rao, 2007)

The problem of pricing, the cost structure and profitability ratios were entrusted to Hathi committee in 1974. The recommendation of the Hathi committee resulted into Drug Policy Control Order 1979 the salient feature of this order are as follows:

1. The returns to be allowed on the bulk drugs coming under the purview of price control were fixed between 12 – 14% post tax on net worth depending on the category of formulations.
2. The new bulk drugs which have been developed through original research and development in India would not be in the preview of price control for the period of 5 years.

3. Introduction of "leader prices" the 1979 Drug Price control DPCO empowered the government to fix "leader price" for majority of formulations. Theses leader prices would be based on cost of efficient manufacturer. All those manufacturers whose prices were above the level of leader prices were required to bring down the level.

The new DPCO which was promulgated in 1987 government took a pragmatic view and adopted a rational growth oriented approach. The next DPCO 1995 contained many positive features as for example:

i. Abolished licensing requirement with a couple of exceptions like genetically engineered drugs.

ii. Raised the equity ceiling for foreign companies from the existing 40% to 51%. The government approval for foreign technological collaborations would also be automatically cleared.

iii. Introduced three criteria turnover, monopoly competition for assessing the drugs should fall in the price control basket.

iv. Replace the existing two lists of 142 price control essential drugs to a single list of 73 drugs. Resulting price control would cover about 50% of retail pharmaceutical market as compared to 70% in the previous list.
The pharmaceutical policy announced in February 2002 reduced the number of drugs under price control from 74 (under DPCO) to about 34. With this the price coverage of the industry would have reduced considerably. (Chaganti Subba Rao, 2007)

4.3.1 Protection of International Patents and IPR

The term 'Patent' otherwise known as Intellectual Property Rights (IPR) plays a pivotal role in the present day development discovery, marketing and pricing in all areas of development, particularly in pharmaceutical field.

A Patent is a set of exclusive right granted by a state to a patentee (the inventor or assignee) for a fixed period of time in exchange for the regulated public disclosure of certain details of a device, method, process of composition of matter (known as an invention) which is new inventive and useful or industrially applicable. (Rajesh Kumar and S M. Satish, 2007)

Currently about 140 countries give legal protection to both product patents as well as process patents as per the Paris convention on international patents and IPR. Recently three more countries i.e. Mexico, Brazil and China have agreed to provide protection to international patents. India has agreed to this when it signed the GATT agreement in Morocco 1994. (Rajesh Kumar and S M. Satish, 2007)

4.3.2. Trade related aspects of Intellectual Property Rights (TRIPS)

The WTO's Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS) attempts to strike a balance between the long-term social objective of providing incentives for future inventions and creation, and the short-term objective
of allowing people to use existing inventions and creations. (Rajesh Kumar and S M. Satish, 2007)

The agreement covers a wide range of subjects, from copyright and trademarks, to integrated circuit designs and trade secrets. Patents or pharmaceuticals and other products are only part of the agreement. The balance works in three ways:

- Invention and creativity in themselves should provide social and technological benefits. Intellectual property protection encourages inventors and creators because they can expect to earn some future benefits from their creativity. This encourages new inventions, such as new drugs, whose development costs can sometimes be extremely high, so private rights also bring social benefits.

- The way intellectual property is protected can also serve social goals. For example, patented inventions have to be disclosed, allowing others to study the invention even while its patent is being protected. This helps technological progress and technology dissemination and transfer. After a period, the protection expires, which means that the invention becomes available for others to use. All of this avoids "re-inventing the wheel".

- The TRIPS Agreement provides flexibility for governments to fine tune the protection granted in order to meet social goals. For patents, it allows governments to make exceptions to patent holders' rights such as in national emergencies, anti-competitive practices, or if the right-holder does not supply the invention, provided certain conditions are fulfilled. For pharmaceutical patents, the flexibility has been clarified and enhanced by the 2001 Doha Declaration on TRIPS and Public Health. The enhancement was put into practice in 2003 with
a decision enabling countries that cannot make medicines themselves, to import pharmaceuticals made under compulsory license. In 2005, members agreed to make this decision a permanent amendment to the TRIPS Agreement, which will take effect when two thirds of members accept it. (Rajesh Kumar and S M. Satish, 2007)

- Continuous advancement in science, new breakthrough in biotechnology, growing participation in the research and development in pharmaceutical sector and the relative strength demonstrated by developing nations have prompted industrial nations to seek stronger protection for their innovations in all countries. TRIPS was brought in with the purpose universalizing the standard, the intellectual property right and frame the roles of the game of the developing countries on par with the developed countries.

- As an illustration the Indian Patent law 1970 recognized process patents and did not give much significance to product patents for pharmaceutical formulations. Thus the developing countries with process patent protection were able to take advantage of the innovations made by early innovators. When a subsequent product is based on an innovation made earlier, the late entrant enjoys the reduction in cost of developing the product. Of the many countries that adopted process patents, developing countries like India, China, Korea, and Brazil have developed expertise to develop new products which were mostly around the earlier innovations of the developed countries.

- According to TRIPS agreement new patents have to be granted in all areas including pharmaceuticals and the effective period of protection is for 20 years from the date of filing the applications. With the implementation of the TRIPS agreement by the most of the developing countries by 2005, stronger product
patent regime will be uniformly applicable among member countries of WTO on pharmaceutical innovations.

- The implications of TRIPS for the pharmaceutical sector are that the patents will be granted both for products and processes for all innovations and patent term will be 29 years from the date of application (compare to 7 years under 1970 act). India had to enforce the new patent laws from January 2005. During the transitional period of 1995-2005 India has to start accepting applications for product patents from 1995 and provide exclusive marketing rights (EMR) for products that were granted patent protection elsewhere.

- The universal TRIPS regime is expected to result from free flow of trade investment and technical know how among the member countries by resolving the barriers that first in the form of differences in the standard of intellectual property. (N. Lalitha, 2001)

**4.4. The Legal and Regulatory Environment**

The legal and regulatory environment is another crucial aspect of a firm's environment that impinges on long-term operations and alternatives. Government regulations of business everywhere have been steadily increasing. Such regulations limit the choices that managers can make and may also affect the profitability of proposed projects. (Chaganti Subba Rao, 2007)

Another area of concern in the legal and regulatory environment comprises the government's attitudes toward profits, investment credits, dividends, etc. The managers who evaluate future projects must take all these aspects into account while making assumptions. The current legal and regulatory environment of the pharmaceutical industry
in India is a result of several statutes enacted over a period of more than a hundred years. These statutes or enactments can broadly be categorized into three areas:

1. Those pertaining to quality control of the pharmaceutical industry such as quality control, safety and standards of all the drugs manufactured and marketed in the county and those imported into the country. All these are under the purview of the Union Ministry of Health (Directorate General of Health Services).

2. Those pertaining to other aspects of manufacture and marketing of drugs such as investment, foreign collaboration, licensing of production facilities, pricing, trade marks, patents, import of capital equipment, raw materials and technology. All these aspects come under the purview of different departments like the Ministries of Petroleum, Chemicals and Fertilizers, Industry, Finance, Law, Commerce and Labour of the Central Government.

3. In addition to Central laws and regulations, there are controls and regulations at the State level. State regulations of the pharmaceutical industry in India can be traced as far back as 1878 when the Opium Act was enacted.

Under this Act, possession, transport, import, export and sale of opium was regulated with a view to restricting its use either as a narcotic or as a drug. Poisons Act, 1919 was the next regulatory legislation, which empowered the government to regulate the possession and sale of any specified poison and the prohibition of import of any poison except under a license. The Dangerous Drugs Act, 1930, the next enactment, vested in the government control over operations relating to all dangerous drugs, including opium.
Some of the more important legislations are listed in Table 4.2. A pharmaceutical seller/marketer should not only be aware of these but should also possess some insight into these statutes and their implications.

4.4.1. Consumer movement

Another important area of the regulatory environment is the consumer movement. Consumer movement is certainly intensifying. Drug Action Committee, Drug Action Forum - while these and other consumer groups, strictly speaking, do not regulate your business directly, they do generate government activity in the affairs of business. Their influence cannot be undermined; nor their importance ignored.

**TABLE 4.2. THE REGULATORY ENVIRONMENT OF THE PHARMACEUTICAL INDUSTRY IN INDIA**

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<td>1.</td>
<td>The Dangerous Drugs Act 1930</td>
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<td>2.</td>
<td>The Drugs and Cosmetics Act 1940</td>
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<td>3.</td>
<td>The pharmacy Act 1948</td>
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<td>4.</td>
<td>The Industrial Development &amp; Regulations (IRDA) Act 1951</td>
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<td>5.</td>
<td>The Drugs and Magic Remedies (Objectionable Advertisements) Act 1954</td>
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<td>6.</td>
<td>The Trade and Merchandise Marks Act 1958</td>
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<td>7.</td>
<td>The Drug Price Control Order 1969</td>
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<td>8.</td>
<td>The Patents Act 1970</td>
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Source: Chaganti Subba Rao, 2007
4.4.2 Monitoring the regulatory environment

It is obvious that you cannot predict the legal and regulatory environment of your business or for that matter any business. But you can certainly try to make some explicit assumptions about it based on careful observation and monitoring. This can influence positively the strategic plans of your business. Consider these examples:

- The Government currently is trying to abolish the loan licensing system in the pharmaceutical industry. The pressure from industry circles has given the loan licensing system a new lease of life for four more years. The reason for the government's decision is to ensure that all manufacturing units implement the Good Manufacturing Practice (GMP).

- According to the Drug Policy, 1987-the Drug Controller of India (DCI) can and most certainly will insist henceforth on the clinical research data of every new formulation by company even if that formulation happens to be a "me-too" product and an existing one. This is to check the ever-increasing brand proliferation. Till now the companies introducing new formulations of drugs already cleared by the DCI needed to submit only the laboratory data pertaining to quality control, stability records, and the like. The new Drug Policy has brought all that changes in a marketer/producer who is alert to changing regulations like these would be better prepared to meet the task of a new product introduction. (Chaganti Subba Rao, 2007)

4.4.3 Regulatory Framework

The Indian pharmaceutical industry has a multilevel hierarchical regulatory institutional framework. Two ministers of the government of India play a major role
in regulating the pharmaceutical sector in the country. Each of these ministers deals with different aspects of regulations and work independently. They are:

1. Ministry of Health and Family welfare (MoHFW)

2. Ministry of Chemical and Fertilizers (MoC&F)

Fig 4.5

Source: www.chemicals.nic.in/pharmalO.htm, 2008
Central Drug standard control organization

The Indian government has enacted a comprehensive Patent Act in 2004 in alignment with the requirement of WTO. The turnaround of the Indian pharmaceutical industry dates back to year 1999, when government of India constituted a committee to lay the framework of R and D in India's pharmaceutical industry and a Task Force for Knowledge based industry. (http://chemicals.nic.in/phaimalO.htm and www.cdsco.nic.in)

It is the responsibility of the government to ensure that drugs to be used by public meet the established standard of quality, safety, biodiversity and efficacy standards of identity, purity freedom from toxicity and strength in respect of every medicine and related products used for diagnosis, prophylaxis and treatments of disease in human beings or animals have to be specified. In India the import, manufacture, sale and distribution of drugs and cosmetic is regulated under the Drug and cosmetic Act 1940 and rules 1945. Under the Act distinct statutory functions and responsibilities have been assigned to Central and state government. The Central drug standards control organization, director general of health services, Ministry of Health and is entrusted with the enforcement of regulatory responsibility at the government of India level. Some of the important activities of the Central drug standards control organization (CDSCO) includes direct interface with R and D activities in pharmaceutical sector at National and international level. The basic function of the regulatory framework is to ensure quality and maintenance of good manufacturing practices.
The Drugs Controller General of India (DCGI)

DCGI is an apex body in the pharmaceutical industry governing issues such as product approval and standards, clinical trials introduction of new drugs and import licenses for new drugs. Its major functions include:

- Laying down standard of drugs cosmetic, diagnostic and devices
- Laying down regulatory measure amendments to Act and Rules
- Regulate market authorization of new drugs
- Regulate clinical research in India
- Approve licenses to manufacture certain categories of drugs as Central License Approving authority i.e. for blood banks, large volume parental vaccines and sera.
- Regulate the standards of imported drugs
- Work relating to the drugs technical advisory board and drugs consultation committee
- Testing of drugs by central drugs labs
- Publication of Indian pharmacopoeia

i.) Regulatory Agencies

It is the basic responsibility of the Government to ensure that drugs to be used by the public meet the established standards of quality, safety, bioavailability and efficacy. Standards of identity, purity, freedom from toxicity and strength in respect of every medicine and related products used for diagnosis, prophylaxis and treatment of diseases in human beings or animals have to be specified. In India the import, manufacture, sale and distribution of drugs and cosmetics is regulated under the Drugs and Cosmetic Act.
Under the Act, distinct statutory functions and responsibilities have been assigned to Central and State governments. The Central Drug Standards Control Organization, Director General of Health Services, Ministry of Health & FW is entrusted with the enforcement of regulatory responsibility at the Government of India level. Some of the important activities of the Central Drug Standards Control Organization (CDSCC) includes direct interface with R&D activities in pharma sector at National and International level. The basic function of the regulatory framework is to ensure quality and maintenance of Good Manufacturing Practices.

ii.) Quality Control and Good Manufacturing Practices (GMPs)

Over the years, the Indian pharmaceutical industry has made significant progress with respect to manufacturing, most of it in requirement of drugs and now exports a significant quantity of medicines of internationally acceptable quality. The quality of drugs has to be closely monitored to maintain standards. (B Rajesh Kumar and S.M Satish, 2007 and Pharmaceutical Policy report 2002)

A manufacturer is obliged to follow the rules provided in Schedule M, the Good Manufacturing Practices (GMPs). A drug is of acceptable quality under the Act not only if it meets the finished product specifications but also more importantly if it is manufactured in a plant complying with GMPs. The responsibility for enforcement of GMPs in respect of most drugs rests with the state drug control authorities but the level of enforcement and competence of
auditing personnel does not appear to be uniform among states. (B Rajesh Kumar and S.M Satish, 2007 and Pharmaceutical Policy report 2002)

In view of the serious problems encountered with certain categories of drugs like blood and blood products, large volume parenterals (LVPs), vaccines, etc, joint inspections are required to be carried out under Rule 68A of the Rules by inspectors of the CDSCO and the concerned State Government before a license for the manufacture of the notified drugs can be granted or renewed by the Central License Approving Authority (CLAA) appointed by the Central Government under the Act. This list is expected to be enlarged as other specialized items like medical devices including transfusion sets; sterile syringes, etc. are notified in this category. (B Rajesh Kumar and S.M Satish, 2007 and Pharmaceutical Policy report 2002)

The drugs controllers of the states are empowered to license the manufacture and sale of drugs in their respective states. Under the Act, the DCG (I) in order to ensure uniform implementation of Rules is enjoined with the responsibility of coordinating their activities and decisions under the Drugs and Cosmetics Act through the Drugs Consultative Committee (DCC). In addition, the Drugs Technical Advisory Board (DTAB), a statutory body under the Act, is required to advise the Central Government and State Government on technical matter arising out of the administration of the Act. (B Rajesh Kumar and S.M Satish, 2007 and Pharmaceutical Policy report 2002)

For a manufacturer intending to export drugs, a GMP certificate under the WHO Certification Scheme on the quality of pharmaceutical products moving in international commerce is the generally accepted norm. The WHO Certification Scheme is a mechanism by which the importing country is in a position to ascertain
whether it has been manufactured in accordance with internationally accepted GMPs. These certificates are issued after joint inspections by teams from the Central and State Governments. Many importing countries, however, lay down their own stringent procedures of inspection and approval of the plant, facilities, manpower, procedures, etc. before a drug manufactured by the applicant is allowed to be imported.

With the growth of the pharmaceutical industry, there has been considerable impetus to research and development activity on drugs. A number of medicines are now exported. This requires proper regulation so that safety, efficacy and quality issues are attended to in a globally accepted manner. This has become all the more important with the coming into existence of the International Conference on Harmonization of Technical Requirements of Pharmaceuticals for Health Use, commonly known as the International Conference on Harmonization (ICH), which promotes scientific and technical aspects of registration of pharmaceutical products.

As a result of adoption of cGMP (code of Good Manufacturing Practices), the number of companies will come down drastically from over 20,000. In China, the cGMP (code of Good Manufacturing Practices) — a structured code that lays down strict manufacturing guidelines) compliance guidelines brought down the number of Chinese pharma firms from over 6,000 to just about 600 today. (B Rajesh Kumar and S.M Satish, 2007 and Pharmaceutical Policy report 2002)

iii.) Registration of Drugs

Most countries of the world, including developing ones, have well-organized system of registration of drugs permitted to be imported or manufactured.
Thus master files of products are submitted for evaluation by the regulatory agencies. It is only after the furnished data has been found adequate that the product is registered in the country. No such centralized system exists in India. There is a need for checking this deficiency by introduction of the registration procedures, which will also help in elimination of sub-therapeutic products. Adequate machinery has to be created in the Central Drug Standards Control Organization (CDSCO) for the purpose.

iv.) Quality Control and Registration of Herbal Drugs

A number of countries including Germany, France, Canada, USA, China, etc. are registering standardized plant extracts of proven clinical efficacy and safety obtained from natural sources as herbal drugs or dietary supplements. In spite of the fact that India has a vast resource of drugs of natural origin, we are unable to exploit the vast world market because we have an unsatisfactory system of their quality control and registration. (B Rajesh Kumar and S.M Satish, 2007 and Pharmaceutical Policy report 2002) On account of the importance of herbal drugs and traditional system of medicines (TSMs) in India, it may be necessary to create a separate division in CDSCO to regulate the quality of such drugs, and to provide proper focus on all related aspects. A system of registration of TSMs, with acceptable standards of quality control and Good manufacturing Practices(GMP’s) need to be put in position.

v.) Approval for New Drugs

A new drug is defined in Rule 122 of the Rules as:

(a) A new substance of chemical, biological or biotechnological origin in bulk or as a
prepared dosage form. A drug already approved by the licensing authority which is now proposed to be marketed with modified or new claims.

(b) A fixed-dose combination (FDC) of two or more drugs, individually approved earlier for certain claims, which are proposed to be combined in a fixed ratio.

(c) All vaccines.

Schedule Y to the Rules specifies the requirements and guidelines on clinical trials for import and manufacture of new drugs. It is a set of comprehensive procedures, the primary objective of which is to safeguard the well being of patients. Thus there is need for proper regulatory and marketing environment, which encourages investment on research and development towards discovery, innovative medicines and promotes their expeditious introduction. The present set-up of CDSCO has not kept pace with the increasing demands of multidisciplinary drug evaluation needs. Applications submitted to the DCG (l) for permission for clinical trials in respect of New Drug Applications (NDA) and abbreviated new drug applications (ANDA) are often referred to outside agencies like the Indian Council of Medical Research (ICMR) and the Department of Biotechnology, Government of India (DBT) for review. This arrangement often leaves very little control with regard to the time runs. In order that the applicant is enabled to complete the investigations in the shortest possible time, it is imperative that adequate infrastructure for fast track clearances is created in the CDSCO. The process of evaluation and review of applications of new drugs needs close collaboration with many organizations like universities, hospitals, industrial associations, professional bodies, foreign and international
There should be chemists/pharmaceutical technologists/chemical engineers to review areas connected with manufacture, in-process control, packaging, stability, purity, and similar parameters of the product. Biotechnology-based and genetically engineered drugs are getting introduced with greater frequency. (B Rajesh Kumar and S.M Satish, 2007) To evaluate the therapeutic effects and adverse drug reactions of a new drug, physicians must be associated in the review process. There should also be adequate number of competent regulatory experts to ensure that not only the requirements of the Act are taken care of effectively but also to guard against the possibility of an over-zealous approach and overshooting the mark. (B Rajesh Kumar and S.M Satish, 2007 and Pharmaceutical Policy report 2002)

Many drugs have serious bioavailability problems. Thus there should be biopharmaceutical scientists available to evaluate data on the rate and extent to which the active medicament in the preparation is actually available to the body as well as on the distribution, metabolism and excretion of the drug molecule.

Association of microbiologists will also be necessary for evaluation of information in case of applications for anti-microbial drugs. Similarly, persons with specialized knowledge in specific areas may have to be brought in for evaluation of the data presented by the applicant. (B Rajesh Kumar and S.M Satish, 2007 and Pharmaceutical Policy report 2002)
India has accepted the responsibilities under the WTO regime. With the Government of India approving the Exclusive Marketing Rights (EMR) route for implementing provisions of the new patent regime, applications for marketing approval will start being received. CDSCO must get ready to meet the situation well in time by creating adequate infrastructure for the critical role it will have to play as a regulatory authority for development of the pharmaceutical sector. (B Rajesh Kumar and S.M Satish, 2007 and Pharmaceutical Policy report 2002)

Pharmacovigilence activities which includes Post marketing surveillance, Adverse Drug Reaction Monitoring etc. is also a critical function of Drug Regulatory Agency. For this, a participative system involving medical community, pharmacists and the industry needs to be developed. These areas appear to have remained neglected. (B Rajesh Kumar and S.M Satish, 2007 and Pharmaceutical Policy report 2002)

Provision of charging fees from applicants for drug evaluation activities also needs to be introduced. This amount can be utilized to meet the expenses incurred in utilizing the services of external experts.

vi.) Continuing Education and Training

We need to review the continuing education programmes so that all categories of staff from the Grade A officers down to the technical assistants get opportunities to upgrade their knowledge by suitable in-service training courses. This is particularly important because pharmaceutical sciences and technology are amongst the areas of fastest growth and development. Benefits from investment in this activity will be intangible in the initial stages but the improvement in the quality of work will ultimately give a sense of satisfaction. It is a common practice in regulatory agencies abroad and by pharmaceutical manufacturers of good standing to organize regular training and
continuing education programmes for their staff. (B Rajesh Kumar and S.M Satish, 2007 and Pharmaceutical Policy report 2002)

vii.) Infrastructure Creation

CDSCO needs to be given an independent status as available to National Drug Regulatory agencies in most countries. These agencies required to carry out multifarious functions but expertise in technical, administrative and vigilance functions is not sufficient. Full-time experts must be there with CDSCO for timely evaluation of the papers submitted by the parties. ( B Rajesh Kumar and S.M Satish, 2007 and Pharmaceutical Policy report 2002)

4.5. Government Policies and Drug Control Orders in India

Various types of controls are imposed on Drugs and Pharmaceutical industry by Government of India from the very beginning. However from time to time they have undergone changes. The industry in India is normally required to pass through following stages of implementation:

1. License
2. selection of product mix
3. finance approvals
4. technology sourcing
5. plant design
6. production
7. price fixation
8. distribution and marketing
4.5.1. Price Control in other Countries

Sale prices of formulations and the prices at which bulk drugs are traded between the parent company and its subsidiaries are regulated by the government of most developing and developed countries. A notable exception is the US of America. (Ministry of Commerce and Industry Department of Commerce Government of India Report, 2008)

Generally speaking, the sale price of a drug is fixed after negotiating with the government. These negotiated prices are usually based on a formula in which the cost of raw materials, expenses on manufacturing, distribution, R and D and profit margins of the producers are included in the sale price. For purpose of illustration, the price regulatory mechanism as prevailing in the UK and Italy are mentioned.

In the UK, a most sophisticated system of price control scheme known as PPRs is in cooperation. Earlier it was called the ‘Voluntary Price Regulation Scheme’ (PPRS). As per this scheme, a manufacturer is allowed to decide his own price for a new product for the first 3 years. After the expiry of this period, the manufacturers are required to negotiate the price of that and also the prices of others sold in the U.K. with the Department of Health and Social Security. The principal basis for price negotiations is the rate of return on investment. It is gathered that this system has worked quite smoothly as it allows the manufacturer to fix his prices as long as the overall rate of return achieves the negotiated target. Another noteworthy feature of this system is that it provides a higher margin of profit to research based companies than to those who mainly produce and sell established products. (Ministry of Commerce and Industry Department of Commerce Government of India Report, 2008)
In Italy, the manufacturers usually fix the sale price to the consumers according to certain established rules. The price fixation is based on the cost of raw materials. Cost of packing materials and manufacturing expenses. A multiple of the cost is used to arrive at the consumer price. The multiplying factor is at a higher rate for research based companies.

According to the Tariff Commission study government did not regulate prices in Switzerland, W Germany, Japan and the U.S.A. However intense competition among manufacturers and operations of the law of supply and demand ensured an effective control over drug prices. Information on the price regulatory system now operating in different countries is not available. According to some, the price regulatory mechanism currently in force in India, extending from the stage of raw materials, finished products and overall profitability of the producers is highly complex and leaves very little freedom or incentive for enlarged production to the manufacturers. The nation’s legal and political environments have a profound effect on pharmaceutical market. (Ministry of Commerce and Industry Department of Commerce Government of India Report, 2008)

After having talked about price, policies and regulation the chapter five reviews the mechanism of development and nature of drug research along with drug discovery process.