Chapter 6

Long-term Perspectives
OPPORTUNITIES & CHALLENGES IN THE GLOBAL PHARMACEUTICAL INDUSTRY

The Major Forces in the Industry:

1. R & D investments have increased rapidly over the last decade or so, far in excess of sales growth, and far in excess of the overall growth in revenues and profitability. Every pharmaceutical company we have worked with is trying to figure out ways to make R & D more productive. This has many implications for the industry in India and I will come to that in a moment.

2. Marketing and sales costs have also increased, Sales-force effectiveness has shown a tremendous drop.

3. Cost containment pressures across Europe, Japan and the US have increased substantially.

4. It is becoming more and more difficult for companies to differentiate on the basis of product alone. There are an increasing number of essentially similar products being produced which are alike in terms of efficacy. This makes it difficult for companies to produces the margins associated with truly innovative drugs.

We will now look at the industry forces in these four areas, R & D, marketing and sales, cost containment, and the basis of competition, in more detail.

R & D:

In R & D, fewer and fewer new entities are being introduced. For the Pharmaceutical Manufacturing Association companies in the US, R & D has grown in real terms from a total of one billion dollars spending about fifteen years ago to eight or nine billion dollars today, but the number of NCEs has remained the same in real terms. (The biotech pipe line is substantial- there are about 130 products under development in biotechnology, so that is going to create a great amount of pressure on the pharmaceutical industry.)
The approval process, whether it is that of the FDA or that any other country, still tends to be onerous and cumbersome and to take a long time. From a development and commercialization standpoint these continue to be pressure for pharmaceutical companies. In marketing and sales there is going to be a trend towards greater promotion of drugs, going directly to the end-users and large institutional buyers with the message. There is a growing amount of interest from the consumer groups as sales effectiveness has deteriorated. This has to be improved: distributors are currently consolidating. Merck paid six billion dollars for Medco, a large portion of this being for their pharmaceutical benefits management process and the ability of Medco to influence pharmacists. In terms of the drugs they can deliver, though, the power of the distributor is going to significantly effect the way this industry functions in the future. PCS, which is a subsidiary of Mckesson, has detailed information on five million people in terms of their drug needs. Medco had twenty million people on their data base. So, buying the data base and being able to influence pharmacists as a result of it is a major source of value-added contribution.

Cost Containment:

A lot of you know about the Medicaid processes, the rebates that they require, the drug related group processes, and the DRRs. Reference pricing occurs most notably in Germany, where, if a product comes off patent and goes generic, all the patented products in the same therapeutic area with the same efficacy have to have comparable prices to the generic price. That obviously impacts the margins.

Co-payment is accruing in a large way in terms of reimbursement in Japan the National Health insurance Scheme has various amendments where prices are forced to decline after the product has been launched.

R & D GROWTH:

let me turn to support some of these notions with data. R & D investments have grown to 20 billion dollars world-wide in an industry with sales of 175 billion. The kick-up occurred around the early 80s. Several factors have driven this increase in R & D. The first is that of more complex/chronic
diseases targets. Most of the easy to address diseases already having been targeted, we are getting into more and more difficult areas. The end-points are less easily defined clinically and often require very long study times and clinical and often require very long study times and clinical trails that can be very expensive, R & D costs grew by 380% from 1981 to 1991 compared with sales growth of 240% and 300% growth in to the companies, or to the producers.

More important, perhaps, is the average cost in the West of developing a new drug, a new chemical entity. It has now gone up to 231 million dollars for an NCE, about half of which are direct costs. This leaves room to reduce costs. Many of our clients have four or five promising NCEs but they recognize that to follow through all five will cost them a billion dollars or two, and they can't afford that, so they focus on just a couple. There is a role that India can play in developing the other two or three. I will address this further as we proceed.

The increasing complexity of new drug development, as I indicated earlier, caused some of the growth in R & D in the '30s, '40s and '50s. This first wave of development concentrated on invasive diseases, and new research addressing viral infections, parasitic diseases, microbial infections. The second focused on degenerative diseases during the '70s and '80s: heart disease, cancer, ulcers, psychosis, and arthritis. Moving forward to the turn of the century, the third wave looks at genetic defects, such as cystic fibrosis and muscular dystrophy, as well as inflammation, and brain disorders. All of these areas are more complex to deal with. They will continue to demand greater and greater focus.

Sales Force Growth:

The other aspect putting pressure on the industry is that prescription sales-force' costs have gone up. Sales force sizes have increased substantially in Europe and the US, compensation and travel costs have gone up, training costs have gone up. Meanwhile, the effectiveness of the sales forces has gone down. Overall ethicals are losing share to OTC and generics. Physicians are writing a much lower percent of all scrips because of the growth of buying groups, clinics and direct mail, all of which have caused the physician to be writing fewer prescriptions. The scrips per physician have
also gone down because the population of physicians has grown faster than the number of patients. Physicians are also very resistant to sales visits. In the west, very highly paid sales people, costing their companies a hundred thousand dollars a year or more, go to the physicians' clinics, and literally do their housekeeping for them, taking away the empty cartons from old samples and putting in new ones. They don't even see the physician. This has been found to be the least cost effective way of doing business.

The number of sales representatives in the US has risen from about 25,000 in 1980, to 35,000 to 40,000 in 1990. In Europe, where we took Germany and France as examples, the number has gone up by about 50% from about 20,000 to almost 30,000 sales representatives. The number of physicians visited per sales rep has, however, gone down because the population of sales reps has gone up at a faster rate. So each sales rep on average visits sixteen physicians in the US and about twelve physicians in Europe. As a result, the dollar sales per sales rep in the US has dropped by about 10%, from 494,000 dollars per rep to about 440,000, over this ten year period. In Europe it has similarly gone down by about 10%. All this suggests that something has to be done regarding sales force distribution.

Cost Containment Pressures:
The cost containment pressures have changed over the period from the '80s to the '90s. There has been a lot of publicity about managed care, but what does this translate into? It translates into a growth in volume discounts because of the concentration of buying power. It also translates to formularies. Formularies are essentially menus where you can pick only one of the drugs on the menu. This acts like a therapeutic interchange where physicians can actually substitute one drug for another, if to their best knowledge the drug to be substituted is more cost effective. This has led to what are called drug utilization reviews, where, in large health maintenance organizations, administrators actually now know how many drugs of a particular type a particular physician is prescribing. This data can be reviewed to see if the physician is out of line in terms of higher drug costs. In the '90s some of these pressures are going to change. There will be growth in Medicaid
rebates. In the US they are now looking at a 8% rebate on the average annual uptake of Medicaid. There are also going to be price caps: one reads about Merck and some other leading companies which have put in price caps linked to inflation. This seems to be a very sound way of pricing in the current environment.

Offshore Tax Returns and De-reimbursement:
The tax credits in Puerto Rico may not continue to hold in the future. A lot of companies have also set up shop in Ireland and some of the tax benefits over there might also change as one moves forward. In Europe, de-reimbursement, which is essentially the removal of products from reimbursement through insurance, has taken place. In the UK, pricing has been effected by a scheme called PPRS, the Pharmaceutical Price Registration Scheme. This limits the profits to pharmaceutical companies to between 17% to 21% as a return on capital employed. The price so regulated is, therefore, based on the returns to the industry. The levels those returns have been set at depends on certain fine points. There is, of course, growing price control in terms of the launch price and also the growth in that price over time.

In the future, you will see in Europe a growing amount of cost containment around the therapeutic proof for new drugs. You will not be able to just introduce a new drug at, say, a new price which is 50% higher than the last one. You will actually have to substantiate the therapeutic proof and that it will yield higher co-payments.

What the industry has done is to shift the onus from insurance companies to the patients in terms of co-payments and reimbursements. What they have also tried to do is to increase the overall efficiency of the industry through DURs, formularies and therapeutic interchange.

The Implication of Managed Care:
In 1988, 48% of the US population was under some form of managed care. That will go up to 81% by the year 2000. Such a major shift in as brief a period as ten to twenty years is unprecedented. It creates a sense of urgency in terms of how drugs are delivered, and also about the opportunities now available to Indian manufacturers- as we take advantage of the low-cost ethos that is going to
be reflected in the public PPO and HMO domains of the industry in the US. It is also becoming
darker and darker to compete. In 1988 if one looks at just cardio-vascular drugs, there were about
hightech marketed products. By 1991 there were 33 marketed products with essentially the same
areas of focus. There happen to be about 150 development compounds solely for cardio-vascular
drugs under way right now. So there is a growing number of essentially similar drugs in the industry
just because it is getting very hard to differentiate.

ALLIANCES

To summarize the forces at work in the industry, I will look at the three eras or decades. The
golden years were the pre-'80s, the consolidation years for the industry were from 1980 to 1990: the
iron years are the '90s, to the year 2000. The basic industry forces in this last period have been the
decreasing productivity in sales and marketing and R & D, and its decreasing affordability. There
were a number of uninsured lives in the Western world. The structure in the 1980s was basically
that of a highly fragmented industry: very local, market driven, with high profits concentrate within
therapeutic area. In the '80s to '90s there has been a spate of consolidation and mergers, there has
been heavy investment in R & D as companies try to out-innovate one another, and there are a
growing number of integrated players who dominate by therapeutic area and geography, as well as
niche providers, and providers that dominate in a particular geography. In the '90s we will see
more withdrawals from the industry, we will see declining profits, and we will see a substantial
increase in the number of alliances. In 1986 there were 40 alliances with biotech companies
world-wide. In 1992 there were 160. The total number of pharmaceutical alliances of various
forms co-marketing, co-development, etc was 120 in 1986 and 350 in 1992. These are tremendous
shifts for a five to six year time frame. Alliances are going to be a fundamental aspect of the
Industry. Why this is important is because there is an
absolute openness from Western pharmaceutical companies to partner with us; to partner with
companies in countries like India, China, Poland, Italy, Mexico. In the '80s there were very strong
Zonal differences in regulations. In the '90s there was a real move towards harmonization. This was
particularly clear in the EU but across the world different countries were looking at others, saying,
let's at least have some basis for being more uniform in how we think about this fundamentally important industry.

Moving Forward:

We believe, moving forward, that price regulation will increase. Probably more importantly there will be a limit to non-innovative products. One just will not be able to introduce a new product with dubious or at best incremental efficacy. As one looks at the other aspects of the changing market, competition in the '80s could best be described as gentlemanly. There was a high degree of unmet need and a variety of competitive profiles with different strategies. In the last decade there has been a real growth in generics and biotechnology and increased competition in niche market segments, Moving forward you will see even greater price competition but, more importantly, truly innovative drugs will be able to maintain a premium. The basis for deciding the price of new innovative drugs is going to change. Historically, pricing has been on what is the best substitute. We believe that in the '90s this will change to what the overall system cost or what the system savings of that drug will be across the entire health-care system because there is a growing understanding of the interdependence of different aspects of the health-care system. So, if there is something that is truly innovative you will be able to get substantial premiums to reflect the system's social savings. The focus on customers has historically been on the physicians. More recently, there has been an increasing influence of peers, hospital administrators and HMOs, and moving forward you will see higher power among institutional customers.

I would like to give you a couple of anecdotes about this. Kaiser Permanente is the largest HMO in the US. They went to Smith Kline Beecham for Tagamet and basically told them that they would put them as an exclusive on their formulary for the drug to be prescribed. Tagamet has now got 66% share of ulcer drugs prescribed at Kaiser and Zantac 33% Whereas Zantac was much more expensive and historically held about 80% of all the drugs prescribed by kaiser, it is now down to 33% because Tagamet has been able to get on the formulary because of the substantial discount they got from SKB as a result of the purchasing power of kaiser.
Medco, which is a huge HMO in insulin, found that Nova was the cheapest source of insulin drugs. They also agreed to put Nova on their formularies. They had Nova sales reps detail the products to their physicians, put up special 800 numbers for immediate assistance on some of the more technical aspects, and trained everyone on chemical equivalence. Now Nova's insulin products account for 95% of all insulin medication prescribed by that HMO. This has reduced the overall cost of insulin drugs for Medco by 50%.

INDUSTRY PARTICIPANTS IN THE YEAR 2000:

As you can see from these trends, there is so much purchasing power here that buying groups can actually go out, cut special deals and force a prescription of these drugs. Our view is that by the year 2000 there are going to be three types of pharmaceutical companies: global, major companies: therapeutic area specialists; and geographic area specialists. Global, major companies will differentiate themselves because they will be in all the major markets, will have a critical mass of skills in every large market, will be very quick to market, and will be good at alliances and cooperation. They will balance their pipeline by licensing in, licensing out, and swapping products to ensure that there is a smooth pipeline of products moving forward. Examples of these companies are: Merck, Bristol Myers Squibb, Smith-Kline Beecham, and Glaxo.

The therapeutic area specialist will dominate market share in a particular niche therapeutic area, will have strong internal R & D, and a very strong external network with academic and other research institutions and perhaps even with some of the R & D institutions that we will hopefully have in India. Again, alliances will be important to them. Examples of such companies are: Astra, Nova, and Nicomed. Geographic specialist will dominate because of a superior sales force, because they understand the physicians and the influences of prescribing behaviour in each market, will have cost effective R & D, excellent regulatory relationships in each local market and licensing of products into a particular market through their world-wide network. There will continue to be high cultural entry-barriers, so the geographic specialists will continue to do well. Sigma Tao, some of
the Japanese and German companies, Marion Merrell Dow, and Rhone-Poulenc Rorer, are examples of this kind of company.

Research boutiques, generic suppliers, and bio-technology suppliers are major areas of growth for the industry. There will also be specialists in how drugs are actually delivered within the body. Alza in California is a very good example of one such company.

PRIORITIES FOR THE NEXT FEW YEARS:

I would like to talk about what the priorities for providers will be in the next five to seven years. As one looks at the success factors for the '90s there are around five major areas. R & D Productivity, as I have indicated, is a real emphasis. This can be broken down into two areas: the innovation of truly new products with high efficacy, and the speed of innovation. In the '80s that was reasonably important, in the '90s its going to be crucially important. Marketing effectiveness is also going to be very important, though was marginally important in the '80s, as all the sales forces continued to grow. In the '90s you will see major reductions. We are talking with companies that are reducing their sales forces by 50%. This sort of substantial reduction will be true across the world during the remainder of this decade, largely as a result of managed care the concentration of buying power.

Operation Effectiveness:

There are two areas of operation effectiveness. One is expenditure. How efficient are you in terms of inventory holding and how streamlined are you from an operations standpoint in chemical and pharmaceutical manufacturing? This was entirely unimportant in the '80s because everyone felt that on this is an industry where such costs are only 15%. In reality, there are substantial opportunities for savings here. The reason for this is the consolidations in, the '80s, two major companies which joined hands now realize that they had far more assets and far more plants around the world than they really needed. I have spent the major portion of the last year in the US meeting with the
Chairman and the President of one of the largest pharmaceutical companies on a regular basis in order to reduce their number of plants world-wide from about 25 to about 10. Now these changes can't happen overnight because of re-registration and regulatory approvals and so on, but they have a three year plan to cut down the number of plants.

The reason that this reduction is necessary, is that there is about 200% excess capacity in pharmaceutical manufacturing among all the major pharmaceutical companies around the world.

Global Reach:

Global reach is going to be essential. More and more companies when launching a new drug are saying that they need to have a global launch. They need to be able to have revenues which come from Europe, Japan, the US and the rest of the world in relative proportion to their market sizes. This is really important because India, I believe, will be able to sell more and more into the global market as a result of this focus. Pharmaceutical companies from the West will try and attempt to launch product into the emerging countries in the Far East and South East Asia at the same time.

Alliance marketing:

Alliance management is going to be a really important aspect moving forward. You will see a growing number of Co-marketing arrangements. Toll manufacturing, which has historically accrued in the industry, will continue. Clinical Trails:

You can now go to third parties to carry our clinical trials for you. You don't have to be a totally vertically integrated company. A representative of a major producers recently said that their company was now doing some stability testing for generic products in India. So there is a showing awareness you can ally with an Indian company, or with a subsidiary in India, and do some of the things that you would normally have done in the West.
Innovation:

Much of the innovation, the growth opportunities and the impact of India is going to be in biotechnology. There were 132 biotechnology drugs under development in 1991, where there has only been some 15 or 20 introduced so far. So there is a huge pipeline that can substantially effect the impact of the pharmaceutical products under development. We compared the bio-tech industry last year to a leading pharmaceutical manufacturer Merck & Co. The entire biotech industry, world-wide, had a equity market value of about 4 billion dollars. Merck's market capitalization was 60 billion. The net income for Merck was two billion and the bio-tech. industry lost three billion dollars in aggregate. However, the bio-tech industry spent five billion dollars on R & D. Merck spent about a billion. The world-wide sales of the entire biotech industry were about six billion dollars compared to Merck's nine billion. The reason we have drawn this comparison is to show you that if you were to think of the biotech industry as one company, it is in some ways now almost the leading company in the industry, and it will continue to grow from here. We haven't even begun to see the potential of this area.

The other major growth opportunity, and India needs to understand how it can take advantage of this, is in drug delivery systems. There are various new technologies based around helper compounds, oral compound release products, and polymer implants, each of which now have companies targeted on trying to find ways to improve the impact and efficacy and efficacy of the drugs through slow-release mechanisms, polymers or enzymes, used to guide drugs which are taken intact to the target within the body, miniature pumps, micro-encapsulated particles, or even nondissolving sponges, all allow slow release. Polymer implants include small polymer wafer and capsules or gels which allow a long-term slow release at local sites. These technologies are all going to offer tremendous opportunities for growth.

Another area of innovation is that around transdermal patches. A widely advertised patch is, of course, the one used against smoking. Alza has taken the lead in skin patches which steadily release correct dosages into the bloodstream, and in microspheres, polymers of fatty compounds which enclose
the drugs and which allow their slow release at a potentially lower toxicity. There is a large number of companies in each of these areas.

The Social Costs of Diseases:

The other reason for growth in the industry is because the social costs to society caused by diseases which have yet to be addressed is tremendous. In the US alone (you can double or treble the figures for the rest of the world), cancer has an annual social cost of a 100 billion dollars; cardio-vascular diseases have about the same; as does Alzheimer's disease. Arthritis, depression, diabetes, and Aids, are all somewhat lower. The level of Aids costs, at fifteen billion dollars, often surprises people who are concerned to find a cure for Aids because they have not looked at the scale of the social cost of Aids compared to other, more established diseases.

There is still a lot of opportunity in terms of opportunity in terms of the areas that are open to innovation, where we can develop new drugs and get ten years of price relief for it.

Generic Drugs

The other vast area of growth in the industry has been the generic drug sector. This is going through a sea-change in terms of what is going to happen through the rest of the century compared to what has happened so far. In 1992, generics comprised about an eight billion dollar industry in the US and thirteen billion dollars worldwide. We expect it to grow to about thirty billion dollars in the US alone. This is tremendous growth rate.

There is one aspect of generics not commonly understood. There are really three types of generics. The first is the drugs, which are essentially patent brands. When a drug, such as Voltare, comes off patent, the original pharmaceutical company will continue to sell it as a generic. This is the major source of revenue. Third-party generics, a new entrant in the industry, will provide this same product. So the off-patent brands will continue to be sold as Voltare. The third-party generics will not be sold by the name of Voltare but by the generic's name. The originator company will sometimes also sell the same product under its original name, but not as the branded products.
In each of these areas you are looking at a 20% growth rate. Why this is important is that in generics you need to be absolutely the lowest-cost manufacturer. India has a substantial advantage here in being able to supply bulk actives and bulk chemicals into that industry. Sitting next to me in the plane as I flew back from Europe recently was a person from Merck coming out to a company on the west coast of India where they were going to source products for generics. So this is happening already and we should find every way possible to take advantage of our ability to provide generic products from India. We only have five or six years before this generic industry really booms, so we have to find a way to get in soon, or else the Italians, the Polish, the Chinese, will win the market race. Some of the reason for this generic growth is that every year, from now through the rest of the century, a number of products will come off patent. Each coming year five billion dollars in revenue from patented branded products is going to come off patent. Typically, when that five billion dollars revenue comes off patent, the price drops by about 50%. So you will then see the generics industry grow by about 2.5 billion dollars with just those products which have come off patent in 1993. In 1994 you will see Seldane and Tagamet come off patent; in 1995 Zantac; in 1996 Rogane, and on and on. On average, through the rest of this decade, you will see four billion dollars of revenue generated through patented products coming off patent, This translates into a growth of about two billion dollars each year in the generics industry. This a tremendous growth.

Obviously this is something that many people have already understood. If you look at the new entrants in the generics industry, in 1993, Upjohn, Sandoz, Rhone-Poulenc Rorer, American Home Products, Marion Merrell Dow, all entered the market. Glaxo, Pfizer, Hoffman La Roche are all actively considering it. Merck entered last year. These are just from among major branded manufacturers which are among the top twenty in the world.

The key success factor in the generics industry, as I have already pointed out, is low-cost manufacturing, using fundamental low-cost ethicals. A number of the Western branded manufacturers do not
know how to do things on a low-cost basis. In India, we do. So we can succeed.

You need an augmented ANDA approval for generics. The total cost of going through this process for a product that’s coming off patent is about one million dollars. So, to be a participant in the generics industry, we need only to spend one million dollars, compared to 231 million dollars for a new chemical entity. I would like to emphasize, however, that if we are to actually participate, we will have to find ways to circumvent some of the infrastructure problems and actually get products to the markets on time.

Focus and collaboration:

All the large companies agree that they have to focus on a particular therapeutic area and on certain disease targets. Merck, being the largest, works across the spectrum from being ace inhibitors all the way through to buying in. Some therapeutic areas they will make major investment in research of over 200 million dollars, in some they will make a minor investment in research, and in some they are going to license in. Companies like ICI have also said that they will only focus on certain therapeutic areas in this case, only on ace-inhibitors and quinolones. There is a growing understanding that companies need to focus and they need to collaborate by licensing-in technology. We looked at Sandoz’s internal versus external delivery discovery, and at what was projected for last year. Of 400 million dollars in enhanced revenue through internal versus external discovery, over 50% of their increase in revenues came from discoveries made outside of Sandoz. They focused on only three areas: immunology, CNS disorders, and cardiovascular. They partnered with institutions like the Dana-faber Cancer Institute or the Institute of Technology, Zurich. This is important because these companies are now willing to partner in discovery and development. Here there is an opportunity. The Institute of Technology, Bombay should be on that list in five years from now. We have worked closely with some of these pharmaceutical companies, putting together their five-year business plans. What is astounding is that of the twenty billion dollars in R & D spending that they are to invest over the next five to seven years, a full
50% of that money will be invested outside the company. This will feed into the world environment; into small companies, into research institutes, into biotech start-ups at a rate of ten billion dollars a year in venture capital. The total venture capital in the high-tech industry in the US today is only four billion US dollars a year. The pharmaceutical industry is going to bring to bring in a cash infusion which is unprecedented. Why can't we in India have two, three, four, or five percent of that ten billion dollars? We have strong reasons for this collaboration: small companies typically need capital, they don't know how to go through the development and regulatory procedures, they don't have marketing capabilities, they focus on value creations through niche roles like discovery, clinical trials, and drug distribution.

Large companies, as I have pointed out, face a decreasing productivity in their own research. They also face an increasing complexity of basic technology development and manufacturing. They have portfolios with, say, ninety products under development, some of these products having absolutely no hope of actually making it to the market. They have to work on their portfolios. As I have pointed out earlier, they have excess capacity and under-utilized assets. The reason for the collaborations between the large companies and the small companies or research institutes is, therefore, cost containment, and because of another big schism that is occurring the increased divergence between the skills needed for discovery and the skills needed for development and marketing. There is a growing awareness that you can go all out for discovery. This works straight into the strengths of India in our role for the future.

I would like to discuss the implications of all these changes and the priorities and pressures facing the industry in the rest of the world. The first implication is that for R&D effectiveness and what India might do for it. We can definitely be the strongest subcontract house for discovery, if we put our minds to it. But this entails a lot. It entails more than just incentives and subsidies from the government. It entails making sure that we have institutes of research and institutes of education, so that we continue to increase our human capital and our intellectual capital. Biotech requires a tremendous amount of labout.
we will not be able to be the nerve-centre for discovery unless we increase by ten-fold the number of trained scientists that we are producing. Only then we will be able to tap into this ten billion dollars of venture capital.

The other area of emphasis that I have pointed out is that of generics and low-cost manufacturing. We can be a source of bulk actives and chemicals, as is evident by Merck coming to India. We need more GMP-approved facilities. We need to find out ways to achieve this. What we actually have is a unique competitive advantage in manufacturing process refinements, unlike the Western world where to go through a process refinement you will have to spend lots of money and go through the entire approval process again. We can make process refinements over here without having to go through some of these cumbersome and onerous procedures. We are, therefore, able to manufacture drugs at substantially lower costs.

Combination drugs are somewhat controversial and I know that some of the purists do not believe in enhanced efficacy in this area. The rest of the world outside the US and Europe is actually very open to combination drugs and there is fair amount of potential there. I was in Mexico City helping a pharmaceutical company there establish its strategy for global expansion. The drugs I was looking at were combination analgesic and anti-inflammatory products, where the efficacy is, in fact, higher. India will be able to tap some of that potential. If Mexico believes that there is a strategy for globalization around this area, India has even more of an ability to achieve this. In looking to the future the last area in which we have a lot of opportunity is that there will be more and more special populations of people, of people who have genetic diseases, people who have high cholesterol levels, depressive personalities, etc., who even relate differently to different drugs. We will be able to carry out demographic efficacy trials much more cost-effectively in India for these sample populations. So, with these thoughts in mind, and leaving you with the urge to actually take advantage of these opportunities in the next two or three years before the window of opportunity is lost.
TREND SCENARIO FOR 2000 A.D.

Type of Society:

Society would still be tradition bound except in the principal metropolitan cities. Literacy would go up (65%) Family Planning measures would still not be adopted by large sections of the rural population. Farming in most parts would still be based on the traditional methods except for the use of chemical fertilizers and hybrid variety seeds.

Population:

Population would have grown to about 960 million of which 26% would be in urban areas and 74% in villages. A population growth rate of 1.9% would be achieved with a birth rate of 2.9% and death rate of 1.0% as family Planning measures would not be effectively implemented in the rural areas. Average life expectancy would be 58 years. Movement of population from rural to urban areas will be mainly due to large sections of people in rural areas living below the poverty line.

National Income:

The economic development of the country would not pick up and sizable population would be still below the poverty line. National income would grow by 4% compound growth rate and would be 2.4 times higher than the present level at constant prices. The per capita income for all India at constant prices would go up by only 55% from existing Rs. 1,163 to Rs. 1,806. This is mainly because of preferred treatment given to public sector despite its unsatisfactory performance. Private sector growth would be hampered because of controls. Licensing delays, capacity restrictions and discouragement of automation in industries with the hope to bring down unemployment. Agricultural production would still largely depend on the monsoons and in large parts, farming would still be using traditional methods except for the use of chemical fertilizers and hybrid variety of seeds. Mechanised farming would be adopted in few parts of the country. Food control measures would still be unsatisfactory and energy supply inadequate both to the industrial and agricultural sectors. Consequently, food production would be marginally short of our require-
ments.

Health Services and Sanitation:

Rural health services would still be inadequate with. One Primary Health Centre (PHC) for every 40,000 population and one sub-centre for every 4000 population. Doctor to population ratio in urban areas would be 1:680, which is equal to the ratio prevailing now in some of the developed countries while in the rural areas it would be adverse at 1:3400. Safe drinking water supply would increase. From the existing 10% to 50% of the villages and sanitation from 0 to around 30% Immunisation against Diphtheria, Tetanus, Peritussis. Polio and T.B. Would cover 30 to 40% of the rural population and 75% of the urban population. Sizable rural population therefore, would not be adequately protected from preventable and communicable diseases. In view of the unsatisfactory sanitation and safe drinking water facilities in the rural areas, infectious diseases vitally interrelated to the environment would not be adequately controlled particularly gastro-intestinal infections, filariasis, malaria, hookworm and infective hepatitis. As the immunisation measures would be inadequate preventable diseases like Diphtheria, Whooping Cough, Tetanus, T.B. and measles would still be common. Anaemia and malnutrition would also have fairly high incidence as large sections of the rural population would still be below the poverty line.

Drug Industry:

In view of the inadequate expansion in the rural health services as the budget allocations for Health and Family Welfare in the ensuing plans are unlikely to increase significantly, the development of the drug industry would naturally be affected. Inspite of the vast potential that exists, the industry cannot expect to grow at a rate faster than 10%. The figure of production at constant Prices may reach at best to Rs. 7,300 Crores giving a per capita consumption of Rs. 76 as against Rs. 14 in 1977/78. In the urban area it would be around Rs. 176 and in the rural an adverse figure of Rs. 40 per capita. At 3% inflation on drugs and 6% on all commodities the figures would be Rs. 158 for All India, Rs. 75 for rural. The ratio of drug consumption to per capita income would be 2.2% for All India. 3.9% for urban and 1.4% for rural areas.
Crisis Points:

Apart from inadequate expansion of the rural health services the other major problems/crisis points that can be identified are:

a. Inadequate fund generation to support a faster growth in view of price/profit controls making the industry rely more on external financing leading to a high debt-equity ratio and sick units.
b. Inadequate development of newer drugs in the country.
c. Lack of funds and other resources to develop basic drugs manufacture on a large enough scale.
d. Inadequate production capacities arising out of licensing delays in the coming 4 to 5 years.
e. Location policy forcing existing units to develop additional capacities in backward districts thereby sacrificing the benefits of large scale production at reduced costs. On the contrary the viability of the units will be in danger, pushing the costs still further.

Possible Achievements:

The achievements which may be possible are:

a. Well developed expertise in the country of pharmaceutical production can take up the challenges of growth. In the first five to seven years, many companies will go in for basic manufacture of many drugs to protect their interests in supporting formulations.
b. With the Government's emphasis on paying more attention to rural welfare, the opportunity for distributing modern medicines to the rural masses can be exploited through Government and semi-Government distribution systems which are in the process of being established.
PREFERRED SCENARIO FOR 2000 A.D.

Type of Society

The society by and large would not be tradition bound but there would be some inertia to change. Literacy would be quite high (75%) and there would be widespread acceptance and use of family planning measures in urban areas and increasing acceptance in rural areas. Modern medicine and facilities would be available in a majority of the villages. There would be improved use of mechanised and modern farming methods and trend towards automation in industries with gradual shift in population to urban areas.

Population:

With the increasing acceptance of family planning measures in rural areas and the availability of contraceptives and gradual acceptance of sterilisation by couples with two or more children. The population would have grown to 880 million. The birth rate would be 2.2, and population growth 1.2%. Average life expectancy would be 66 years. Movement of population from rural to urban areas would take place because of good industrial growth in cities and towns and increasing usage of mechanised farming resulting in urban to rural population ratio of 30:70.

National Income:

The national income would have a fairly high growth rate of 6% with the gradual removal of price control and other restrictions on the growth of industries. Liberalised policy on licenses and capacities to Indian sector, gradual switch to automation in selected industries, import of technology in expedient cases for the manufacture of sophisticated items. On the food front the country
would be more or less self-sufficient with the gradual usage of mechanised farming methods, flood control measures and irrigation schemes. The national income would be 3 1/2 times higher than the present income at constant prices. Per capita income would go up from the existing Rs. 1,160 to Rs. 3,000. In urban areas it would be Rs. 3,900 and rural Rs. 2,600 at constant prices.

Health Services and Sanitation:

Rural Health Services will cover most of the rural areas, with one P.H.C. for every 20,000 population, upgrading one out of 3 to rural hospital. There will be one sub-centre for every 2000 population with a qualified doctor. Each of the sub-centres will stock contraceptives and drugs to treat common ailments, vitamin deficiencies etc. School children will be supplied vitamin A & D pills free of charge by the State.

Immunisation against DPT, Polio and T.B. will cover at least 90% of the urban and 66% of the urban and 66% of the rural children. Safe drinking water facilities will be available in 90% of the urban areas and 80% of the rural areas. Sanitation will be provided in 90% of the urban and 60% of the rural areas.

Doctor to population ratio will be 1:630 in urban areas and 1:1600 in rural areas.

The per capita drug consumption would go up from existing Rs. 14 to Rs. 150 at constant prices. In urban areas it would go up from existing Rs. 60 to Rs. 250 and rural from Rs. 2 to Rs. 110. At 3% infection on drugs and 6% on all commodities, the figures would be Rs. 268 for All-India, Rs. 446 for urban and Rs. 190 for rural. The ratio of drug consumption to national income would be 2.7% for All-India, 3.4% for urban and 2.2% for rural, based on 3% inflation on drugs and 6% on all commodities.

Diseases:

As the safe drinking water facilities, sanitation and immunisation programme is extended to
majority of the urban areas and high percentage of the villages, infectious and communicable
diseases would be practically eradicated in urban areas while in rural, its incidence will be
brought down considerably. Vitamin A deficiency, anaemias and malnutrition will be uncommon
with the growth in rural income. Lower birth rate and adequate food.

In urban areas incidence of infectious and communicable diseases would be very negligible.
However, ailments and disorders associated with urban life and old age would have a higher
incidence such as psychotic and cardio-vascular disorders. Rheumatoid arthritis, diabetes, bron-
chitis etc.

In rural areas, incidence of preventive diseases would be low because of higher coverage
of immunisation. Infectious diseases such as diarrhoea, dysentry and parasitic infections would have
a fair degree of incidence. Demand for vitamins and anti anaemia preparations would be fairly
high with the growing awareness of health standards.

Drug Industry:

The drug industry would have a fast growth rate of 13% by volume aided by a fairly good
rise in national income increasing both the urban and rural per capita incomes, extension of health
services, transportation facilities to cover majority of the villages and growing health conscious-
ness. The formulation output would go up by 13 times from the existing Rs.900 crores to
Rs.13,000 crores at constant prices. The consumption in rural areas would go up by over 70
times and in urban by 7 times from the existing level. The urban to rural ratio for drug consump-
tion would be 50: 50.

The fast growth of the drug industry takes place because of the encouragement and certain
facilities provided by the Government.

1. Price restrictions would only be on essential drugs to enable the industry to have adequate
   profits and build up funds for expansion.

2. The industry would on its own minimise the inflation on drug prices with increased volume of
   production and adoption of improved processes.

3. Capacity expansions would be allowed on merits of the case.
4. Licences for new drugs and new products would be processed without much delay.

5. Import of sophisticated technology and new drugs and new drug delivery systems would be allowed on merits.

6. Indian sector of the industry would be allowed to expand liberally.

7. Public sector would be expanded as a corollary to private sector.

8. Location policy would be relaxed permitting companies to expand existing capacities at existing locations, based on merits.

9. Allocation for Health and Family Welfare would be increased from the existing 0.3% to 0.45% of the national income.

10. Communication facilities would be expanded to facilitate distribution of medicines and essential commodities in rural areas.

11. Short term licentiate courses would be initiated to increase the number of doctors and facilitate their movement to rural areas.

12. All the major drug companies would be setting up R&D units and working on applied research and development of improved processes to cut production costs.

13. Exports of both bulk drugs and formulations would increase to developing countries and technical know-how too would be provided to these in setting up drug industries.
BULK DRUGS PROJECTIONS

Introduction:

In drawing up the projection for bulk drugs requirement for the year 2000, it is obvious that the objective is to bring medicines within the reach of the common man. The nature and quantity of medicines required would depend upon the disease pattern which is dependent to a certain extent on the lifestyle of people, hygienic conditions, pollution and preventive health measures. Keeping in view the present changes of lifestyle due to industrialization on the one hand, and people living below the poverty line in unhygienic conditions on the other, there is likely to be an increase in the following diseases:

a) respiratory:
b) cardiovascular:
c) hypertension:
d) rheumatism;
e) gout:
f) muscular pain and inflammatory conditions;
g) diabetes:
h) psychosomatic;
i) allergy (side effects caused by the use of modern drugs)

Bulk Drug Requirements:

From Table 1 it is evident that the requirements of bulk drugs for the year 2000 will be at least 8 times as compared to the present requirements considering that the present trend of drug consumption continues (trend scenario). But in case the national income grows at a compounded growth rate of more than 4%, the requirements of bulk drugs could go as high as 18 times as compared to the present requirement.

To produce bulk drugs to meet the requirements mentioned above, we have to consider the questions pertaining to availability of proper technology (improvement/development/import) for the production of bulk drugs and their intermediates, technology transfer and its assimilation by way of in-house research and development involvement, quality assurance, process control and raw material availability and raw material specifications. Before proceeding further on the technology aspects, it
is not out of place to review the current status of bulk drugs production, the technology involved and various constraints which are inhibiting the growth of the industry.

Present status of the Bulk Drug Industry Industry

In India, we have a well established base for the manufacture of bulk drugs and excellent technological support in terms of highly skilled technical personnel. The bulk drug requirements in 1977-78 were met by the production of drugs worth nearly Rs. 150 crores and import of nearly Rs. 57 crores. Approximately 90% of the bulk drugs were produced by formulators and nearly 10% by those engaged only in bulk drug production.

The phenomenal growth of the bulk drug industry during the last two decades indicates that the industry has a potential of expanding and meeting the future needs of the nation. But there are certain constraints as indicated below which are affecting the growth of this industry:

1. Policy regarding import of certain sophisticated technology not available in the country.
2. Premature claims on development of technology and pressure for adoption of such technology.
3. Scarcity and high prices of raw materials.
4. Shortage of power, furnace oil etc.
5. Licensing procedures and delays.
6. Lack of understanding and coordination among Government agencies regarding priority to be accorded to drug manufacturing units for supply of power and raw materials such as alcohol etc.
7. Unsatisfactory quality and delays in the availability of the production equipment.
8. Lack of coordination among various research and process development institutions to avoid duplication of work.

In spite of various constraints, the record of growth of this industry has been excellent. The production of bulk drugs in 1978-79 is estimated at about Rs. 200 crores and the Government estimates the production to go to Rs. 475 crores by 1982-83.

Technology:

The production of bulk drugs is a highly sophisticated field which is continuously supported by research and development efforts. The technology used today in the manufacture of bulk drugs is the one based on petro-chemicals, which is becoming increasingly expensive. The dominant question in this decade undoubtedly will be that of petroleum. Where will the crude oil stock come from, in
India today with a huge sugar industry should maximise the production of ethyl alcohol and exploit fully the production of alcohol based chemicals.

The isolation of chemicals from coal tar is once again gaining importance abroad and we should follow the lead. Regarding chemicals from coal, BASF (West Germany) have made considerable progress in the production of olefins from coal via methanol. This technology from the so called C1 chemistry will one day bridge the gap between coal and petro-chemistry.

In India, with a vast coastline, efforts should be expended to screen chemicals from marine sources. it is likely that some key intermediates can be isolated which could be exploited commercially.

Import of Technology,

The development of technology is a long term process and may often prove impossible. Till the time indigenous technology is developed appropriate technology wherever necessary should be bought on outright basis. In certain instances purely on technology grounds the technology developed in the country may be suitable technically but not commercially exploitable. The result is that the country faces shortage of life-saving drugs. we have therefore to bear in mind that under such circumstances there has to be a trade off between indigenous technology which is not economical and imported technology which is commercially viable and which can provide life saving drugs to the masses at reasonable rates. In cases where technology is to be imported for a variety of reasons it is necessary that we keep pace with indigenous efforts in assimilation, absorption and improvement of the technology. To illustrate the point one can cite the example of production of steroid drugs. These products can be prepared far cheaper from androstenedione (AD) and androstadienedione (ADD) route than by following the diosgenin route. AD and ADD are produced economically by fermentation of sitosterol. By importing the fermentation technology for production of steroids, the steroids based drugs can be made available much cheaper.

To avoid indiscriminate import of technology and duplication in the import of technology, the applications for import of technology should be screened by an expert committee in which at least one or two members should be from the drug industry who have considerable involvement in the development and transfer of technologies. It is an obligation on the part of the experts committee to see that only the latest and appropriate technology is brought into the country. This committee should also involve people already engaged in the manufacture of the concerned drugs in the country.

Regulations of Pollution.
Because of the introduction of pollution laws for the safety and improvement of the environment, the new technology developed should cope with the regulations. At the same time efforts should be expended to improve the existing technology which should comply with the pollution regulations. It is a challenge to R & D executives and they should learn to adjust to the regulatory strictures.

Equipment:

By the year 2000 it will become essential to convert some of the batch size processes into continuous processes. Emphasis will have to be gradually on safety and conservation of energy. As discussed earlier, in process improvement/development, the objective in the plant design should be based on the use of safer raw materials and intermediates and mild conditions with respect to temperatures and pressures. This would help in avoiding a number of problems rather than solving the. The micro-computer control techniques will be gradually diffused in many process equipments. Increased use of automation underlines current concern with plant safety, both in terms of explosive hazards and of exposure of plant workers to hazardous chemicals.

Equally important is the role of process control equipment in the manufacture of bulk drugs. In order to manufacture the drugs of high purity as per international standards, more sophisticated instruments equipped with micro-processors will become essential in process control and quality assurance.

Imports:

the figures for import of drug intermediate for the last three years are given below:

1976-77 : Rs. 3873.12 Lakhs
1977-78 : Rs. 5772.65 Lakhs
1978-79 : Rs. 6272.73 Lakhs
1982-83 (estimated) : Rs. 15000.00 lakhs

These figures can be easily contained or even brought down provided restrictions on production and licensing and relaxed. Better economic sales of production and competition will also result in the development of better technology, which is once again in the national interest.

At this point it may be mentioned that it is not essential to make each and every product in the country. Compounds required in less quantity can be imported. This will save the development efforts and prove more economic than producing just a few kilograms of the drug.
As a consequence, the importance of research and development to drug manufacturers becomes crucial. In order to fulfil our commitments to the nation for the production of bulk drugs there is an urgent need for concerted research and development efforts in national laboratories and in the research and development laboratories of the private sector as well as public sector companies. The proper coordination of the research and development efforts in the various laboratories will avoid duplication of R & D efforts and help the nation in developing processes to fulfil the future needs. Efforts have to be expended in improving the existing technology which should result in conservation of energy, better utilisation of the plant capacity, maximising the use of raw material, minimising use of solvents and in making the processes safer. If we can improve our processes and design our plants based on safer raw materials and intermediates or use of hazardous chemicals where necessary at low temperature and pressure then a number of problems can be avoided rather than solving them. Catalysis, for example, has become a more popular area for process improvement. Using catalysts it has been possible to eliminate the use of hazardous chemicals from certain processes. As a consequence, processes have become safer and economical by eliminating/minimising the use of solvents which are becoming more expensive. The exercises emanating from these applications of the current literature, besides improving technology, also prove intellectually stimulating to R & D personnel. Projects intended to conserve energy and simplification of technology is the need of the hour.

with petro-chemicals becoming expensive, extensive research efforts should be directed both in government as well as in private sector to look for alternate sources of raw materials used for drugs which can be explored in (a) plant kingdom, (b) marine sources, and (c) coal.

In India with huge natural resources, efforts should be expended to utilise natural products as raw material. For example, in the production of 1-methyl dopa, the choice of starting raw material should be naturally occurring eugenol or methyl-eugenol rather than vanillin and nitro-ethane which are imported. Similarly process development efforts should be directed for development of technology for the isolation of gallic acid from gall nuts which can be converted, by a sequence of reactions, to trimethoprim. Isolation of pure solanesol from tobacco waste should be fully explored which could be exploited for the production of co-enzyme Q-10.

The quantity of commercially important natural products in the plants can be increased by undertaking extensive cytogenetic studies.
Incentives:

Whereas the scientists and technologists of the country are willing to accept the challenge of import substitution to meet the requirements of bulk-drugs, there is something that the Government can do to encourage research and development in the country by providing the following incentives:

a) Once a bulk drug is produced in the country will inhouse R & D effort, there should be a five-year holiday from price control. The import of the bulk drugs developed or their intermediates should be banned as long as the cost of production is reasonable.

b) All R & D laboratories (inhouse or otherwise) recognised by the Department of Science and Technology(DST) should be permitted a weighted tax deduction (133.3% exemption) on the expenses incurred on process development/improvement. Separate accounts can be maintained for the expenses incurred on process development/improvement and expenditure on scientific research on activities relating to the existing business of the Company.

c) Recognized R & D laboratories (inhouse or otherwise) should be encouraged to accept sponsored research projects and the sponsoring institution should be permitted a weighted tax deduction (133.3% exemption).

d) There should be no discrimination for investment allowance for exploiting the know-how developed in the country in an inhouse R&D recognized by DST in the private sector, or in a R & D Laboratory of public sector or Government laboratories.

e) Customs Duty Exemption- All equipment and raw material imported for process development should be exempted from import duty. Thus, more funds would be made available for updating technology in a relatively shorter time.

Role of Small Scale Industry

The small scale sector is playing a very important role in fulfilling the bulk drug requirements of the country. There is no dearth of highly qualified and skilled technocrats who must be encouraged with suitable financial and other incentives to expand their activities in the field of bulk drugs.

Suggestions for Achieving Production Requirements And finally, to produce bulk drugs to meet the nation's requirement, the following suggestions are made:

1. Production of bulk drugs should be rationalised.

2. Production should be on an economic scale to provide drugs at reasonable prices.

3. Power, furnace oil, and raw-material such as alcohol etc., which are controlled by Government
agencies should be made available to drug manufacturers without cumbersome procedures.

4. A Committee to identify technological gaps should be set up leading to timely decision on whether technology is to be locally developed or imported.

5. A technology information cell should be set up to avoid unnecessary development efforts.

6. Import of basic raw materials and process equipment should be liberalised.

7. A Vigilance Committee of the drug industry should be constituted to monitor implementation of bulk drug production.

8. In-house R&D laboratories should be further promoted for the development and improvement of technologies.

9. Efforts should be expended to explore alternate sources of raw material.

10. Good manufacturing practices should be adopted to assure acceptable standards of quality of drugs.

There are nearly 600 drugs in use today. Nearly 90 drugs have been selected for the purpose of drugs requirement in the years 1990 and 2000. The list of drugs along with their requirements and the projected annual growth is given in the following table. These requirements are based upon the trend scenario.

R & D discovery and development of new drugs in India will largely depend on a number of factors such as investment in terms of infrastructural facilities, scientific manpower and critical evaluation of the needs of the country. These factors, in turn are related to health services and sanitation and availability of the safe drinking water to the whole of the Indian population. The attitude of various drug regulatory authorities would also influence the development of future drugs.

R & D potential for future drugs

The trend scenario in respect of population health services and sanitation and disease pattern may be visualised as stated earlier. In respect of R&D, the scenario can be visualised as follows:

R & D potential would logically increase because of the need for self-reliance. Almost all the major drug companies would be setting up R & D units. The main endeavour of these units would be on applied research and the development of improved processes to cut down costs. The environment for R & D on drugs will depend on the social pressures for increased drug safety. Drug regulatory agencies will play a significant role in monitoring these pressures and will apply
stringent control measures. This will lead to increased costs of drug discovery and development. The innovation cycle will be longer than earlier years. As a result of increased controls, there will be technological inhibition.

Price increase will be sought to cover escalated costs of development. This will lead to higher operating costs of health services.

The basic strengths and weaknesses of the present R & D environment in India can be stated as follows:

Strength:
1. Excellent scientific manpower and educational institutions.
2. Excellent growth of the drug industry in the past 30 years.
3. Potential to expand and meet the needs of the growing population.
4. Well established base for the manufacture of new drugs and formulations. Availability of a variety of equipment and machinery suited for the development of such drugs.
5. Well organised drug regulatory agencies.
6. Fiscale support for R&D expenditure by Government of India.

Weaknesses
1. Inadequate investment and resource generation to support modern drug research.
2. Current R & D effort for development of new drugs is insufficient.
3. Difficulties in obtaining sophisticated technology from the highly developed countries.
4. Overall Government procedures are cumbersome, time-consuming and bureaucratic.
5. Inadequate supply of intermediates and chemicals required for the synthesis of new compounds to be screened for various activities.
6. Uneconomical scale of production of basic drugs and intermediates.

Realising these strengths and weaknesses of the R & D environment, it would be appropriate here to discuss the preferred scenario for 2000 A.D. in respect of future drugs.

Scenario for 2000:
The future of R&D on drugs will depend upon the health services, sanitation, population control, disease pattern and various other parameters such as the structure of the drug industry itself in India.

There are over 300 new drug entities which have reasonable chance of survival during their future
development. It is difficult to imagine new breakthroughs in drugs originating in this country. However, large scale adoption of new technology developed elsewhere is foreseen. A few events that are likely to occur in R & D with respect to new drug development are as follows:-

1. The most important task for pharmaceutical R & D in India is to produce a reasonably non-toxic, inexpensive contraceptive with little or no side-effects. Although, to develop a non-steroidal, antifertility agent which has the above advantages, is a tall order, the problem is likely to be solved by the development of female contraceptives with one year activity, introduction of sex education in schools and development of post-coital medicines. A male antifertility agent will also appear on the scene.

2. Drugs to control personality traits may become a reality by 1996 and this will have a high impact on our society.

3. Significant process will be made towards the development of intelligence improving drugs by 1990.

4. Development of hepatitis vaccine or a cure for jaundice is foreseen.

5. Development of broad spectrum antifungal drugs are envisioned.

6. Drugs available for curing Schizophrenia will be available by 1995, although new drugs of purely Indian origin for curing depression, anxiety and tension would be available by 1985.

7. Similarly, potent drugs in the field of amoebiasis, trichomoniasis and helminthiasis are likely to emerge from Indian research laboratories.

8. Major development in the treatment of malaria and filariasis is foreseen.

9. There will be a whole new range of semi-synthetic antibiotics directed specifically towards the individual bacterium, fungus or virus. For example, a specific antibiotic for Pseudomonas infection would be a reality by 1985. The role of synergistic antibiotics will become prominent. Sulpha synergist will reach a peak period by 1990.

10. A new development in the field of rationalisation of various systems of medicine (Ayurvedic, Unani and others) is forthcoming. A synthesis of Indian and Western systems of medicines is not ruled out. Thus an emergence of an 'Allovedic' system is foreseen.

Some other conclusions:

The complete eradication of cancer, venereal diseases and diseases associated with malnutrition iron and B-Complex anaemias is not foreseen. Complete eradication of malaria, filaria and trachoma is not likely either. However, the eradication is foreseen of Vitamin 'A' deficiency, tetanus,
diphtheria, plague and small-pox, inspite of the recent reports of the complete eradication delivery systems. Development of the health care in the country will be vastly improved in the year 2000 A.D. Rural health services would have picked up momentum. The primary health care centres would be freely staffed and would have adequate supply of medicines. Education of the people to develop a positive attitude towards disease prevention will be continuously stressed. Drugs with multiple activity to deal with multiple disease states will become available. In conclusion, better health care services, better education, better food consumption will all lead to a healthy and productive population in India in 2000.

Action plan for current decisions to transform preferred scenario to reality

1. For effective control of population, in addition to intensive IUCD campaign, regular use of oral contraceptives is a must. All companies producing anti-fertility drugs must be encouraged to the fullest extent possible.

2. Development of Fermentation Technology as a source for the manufacture of various chemicals in addition to antibiotics. The production of 6-APA and 7-ADCA had to be a stepped up considerably.

3. Process R & D occurs when the need and opportunity arise. Market imperfections coupled with increasing demand tend, to encourage product oriented oriented R & D. Process R&D increases, operational efficiency while new product R & D increases strategic efficiency. The public interest in India will be best served by continued, rapid increase in number of more potent, more effective and less toxic drugs.

4. The establishment of four major regional research centres jointly with drug industry would be a desirable step. These should be located in different parts of the country. Each should have clear-cut objectives and should be accountable to its Governing Council. The main tasks of these centres should be adapt technology developed elsewhere and they should be preferable self-supporting. These centres should also work in priority areas of chemotherapy, toxicology and clinical evaluation.

5. The establishment of a Drug Information Centre will play an important role for the development of small scale sector.

6. Development of immunising agents to protect against protozoal, bacterial and viral diseases should be undertaken.
7. The creation of National Pharmacy Service will go a long way towards the distribution and control of ethical pharmaceutical products.

8. Lastly, the establishment of an Indian Academy of Pharmaceutical Sciences will be a big step towards enhancing the status of drug research in India.

Although, these points barely touch the problems of future, they indicate the desirable trends for tomorrow.

QUALITY ASSURANCE AND GOOD MANUFACTURING PRACTICE

It is worthwhile to keep our ideas clear on the definitions of various terms involved when we talk about Quality of Drugs. As defined in the U.K. Guide to Good Manufacturing Practice 1977:

Quality Assurance: Quality assurance is the sum total of organised arrangements made with the object of ensuring that the products will be of the quality required by their intended use. It is involved with the control at every stage of the life of a product, from the time its ideas and rationale is conceived, through design, development, good manufacturing practices, distribution, storage, till the time the dosage form is administered. Life period of a pharmaceutical product may be conveniently divided in 3 stages.

(i) The development of the drug, animal and clinical testing, formulation and eventual registration,

(ii) The control of its routine manufacture, and

(iii) The continued control once the product has left the manufacturer's care.

Good Manufacturing Practice (G.M.P.): Good manufacturing practice is that part of Quality assurance aimed at ensuring that the product is consistently manufactured to a quality appropriate to their intended use. It is thus concerned with both Manufacturing and Quality Control Procedures, While the primary purpose of G.M.P. is protection of the consumer, the secondary benefits include aid to the manufacturer, improved efficiency and some common ground for discussions between the regulatory bodies and industry.

Quality Control:

Quality control is that part of G.M.P. which is concerned with sampling specifications and testing, and with the organisation, documentation and release procedures which ensure that the necessary
and relevant tests are in fact carried out, and the products not released for use of sale/supply, until the quality is judged to be satisfactory. "Quality Control" is also used in the sense of the organisational entity which has the responsibility of these functions.

A lot of work has been done in the development of the methodology in Quality Assurance with specialised scientific techniques. There is a need for precisely defined and acceptable specifications, chemical, Physical and Biological aspects of control, new concepts and standards for newer drug-delivery systems, storage and stability problems, bioavailability testing, submissions to regulatory bodies. Good Laboratory Practices, technical problems in evaluation of precision of testing methods and so on, which would require getting together of the authorities and the industry at technical courses and seminars to arrive at a consensus of opinion and update the knowledge of all concerned.

For the present purpose of the current status, future trends and preferences it was felt worthwhile to concentrate on the following 5 major areas in the field of quality-control:

1. Role of Pharmacopoeia,
2. Instrumentation,
3. Drugs control authorities,
4. Pharmaceutical aids,
5. Testing facilities.

Role of Pharmacopoeia

WHO in 1953 defined pharmacopoeia as "a pharmaceutical standard rendered mandatory by the competent authorities" and "Standard which gives every safeguard to the patient and the medical practitioner". "It leads to the improvement of the manufacture of drugs and to the discipline of the trade of pharmaceutical products". Pharmacopoeial standards should not be considered as manufacturer's release specifications but minimum standards with which a small sample of the product must comply when applied by an independent examiner throughout the life of the product. Let us consider out Indian Pharmacopoeia. The first edition was in 1955, the second one in 1966, a supplement was issued in 1975 and a committee had been formed in December 1978, yet to start work seriously on the 3rd edition which, with some luck, may be expected in 1985. Pharmacopoeial work involves a continuous control of results, elaboration of new analytical procedures and intense experimental and editorial work.
The facilities for sophisticated testing available at National laboratories are not organised well enough to be of commercial use to the industry, an aspect which needs to be rectified. Various standards required in the analysis are not available and the future I.P. commission will hopefully take care of this situation. Smaller companies will find it impossible to invest in very expensive analytical instruments. There could be an emergence of cooperative testing laboratories. More private testing laboratories are coming up and this trend will continue, particularly with respect to the sophisticated technique of analysis.

Some of the other recommendations are as follows:

Loan Licence

There is a trend in the thinking of the authorities that the system of loan should be discouraged and the loan-licensees must set up their own units with complete quality control systems including full testing facilities. The loan licence system be allowed to continue, whereby the manufacturing and testing is done at expert approved units, until the turnover of the loan Licensee is sufficiently large for him to set up a unit with full facilities of his own. It is not the total number of manufacturing units but the quality of such units which is of paramount importance in future.

BIOAVAILABILITY

The study of the subjects of bioavailability, bioequivalence, therapeutic equivalence of generics and different brand named drugs needs immediate attention. A suitable in vitro model test is the need of the hour as the workload in terms of human volunteers and expense required is quite unthinkable and impractical except for a very few select unavoidable cases. Another factor to be studied is a variation of effects of drugs in people from different parts of a vast country like India where the difference could be as important as in the cases of people of different countries.

Sophisticated testing Facilities:

There are a number of sophisticated instruments centres in the country the working of which needs to be streamlined on commercial lines so that the industry can make timely use of these, leading to mutual benefits.

Good Manufacturing Practices

There has to be more emphasis on making a product in the correct manner rather than testing the final product. G.M.P. must be incorporated in the Drug Rules and, more important, should be imple-
mented by the Central/State Drug Control Authorities. A beginning can be made with parenteral preparations with uniform implementation of G.M.P. in all the States. Once this is done, the quality will follow automatically.

Indian Pharmacopoeial Commission

It is high time the industry and the associations made concentrated effort to get a pharmacopoeial commission established to be able to have an up-to-date national pharmacopoea. This need will become more and more urgent as the production increases for domestic rural markets and also for export markets where we need a better image for the national standards.

Vigilance Committee

The setting up of a vigilance committee for establishing a code of conduct and helping in keeping the high standards of quality of the product manufactured by the industry may be considered.

Analysts Conferences

Regular meeting between Government Testing Laboratories, approved laboratories and private manufacturers’ laboratories should be regularly organised to discuss the latest methods of analysis as applicable to pharmacopoeal products. Since there is a long delay between the I.P. editions, the pharmacopoeal methods, which are the only official ones in the case of disputes, may be out of date and can create problems.

Insurance

In future, insurance for damages to be paid by a company in case of ill effects of a drug or formulation may become an important issue. The insurance companies may insist on precaution of G.M.P., etc., during the manufacture before arranging the insurance and paying the claims.

Qualified Pharmacists

Considering the type of growth envisaged and a wider rural distribution, we need a large number of qualified dispensing pharmacists and manufacturing pharmacists to be in charge of hospitals where a certain amount of manufacture is inevitable. By 1985 Maharashtra for instance would need 6000 dispensing diploma holders in pharmacy against the present availability of 2500. As more and more rural hospitals will come up in future it is important that the manufacture of drugs must be under some control, which is not able quality assurance system exists.
It would be useful to know the details of the defects and do a critical study of the data so that corrective measures can be adopted.

There are about 1500 drugs manufacturing units in our country. Out of these there may be hardly 200 or so who would be involved in parenteral and important biological preparations. The remaining 1300 units may be in the so called small scale sector. There would be out 3000 Iban License units. As far as quality is concerned the sectoral differences like small scale, large scale, multinational or public sector do no apply. A pharmaceutical product must be of a minimum high level of quality and even the smallest manufacturer must have a suitable system for quality control and G.M.P.

The present drug regulatory systems are not uniform all over the country. This is a very serious lacuna in the quality system, as there is insufficient control in certain States and different decisions from the authorities regarding approval of products and combinations. Can there be a system whereby the inspections for approval of manufacturing facilities can be carried out by a joint panel of inspectors from the centre, and the State particularly for parenteral products? In the States where the administration is not built up, the central drug control authorities should exercise the control or it could be done on a regional basis. The regulatory agencies in future would need a lot more work, chemical, pharmacological, toxicological and clinical, to be carried out before introduction of a new product, with a greater emphasis on safety and efficiency. Some of the older established drugs will be withdrawn as fresh review of safety and efficacy is made. There must be a greater liaison between the regulatory authorities and the industry on these issues and an Association like IDMA would have a much larger role to play in the future. Hopefully there would be active ingredients, the Pharmaceutical aids or excipients, which most of the time form a large percentage of a dosage form, deserve greater attention than given till now. The minimum pharmacopoeia standards are often inadequate. There are extra specifications adopted by some companies which would ensure factors like bio availability and stability of the active ingredients safety from chemical and microbial contamination and others. These standards need to be looked into and if these cannot be incorporated in the pharmacopoeia a separate companion book of standards, specially for pharmaceutical aids should be considered. This type of work has been carried out in Switzerland and at present U.S.A. and U.K. are working on a collaborative basis to bring out the specifications for some 150 items of excipients.

Just as for dosage forms, quality must be built in the active and non-active bulk materials
during their manufacture and there should be some provision for inspection for the practice of G.M.P. in their production. In the case of non-active ingredients there is a serious problem of enforcement of required standards as the pharmaceutical industry forms only a minor consumer of the total production and the manufacturers are not economically interested. Again we have to recognise two types of excipients: (a) materials produced for and by the food industry for which standards are expected to be high, and (b) materials produced by or for other industries. The pharmaceutical manufacturers of the future have to arrange inspections and standards of their own to obtain assurance of quality of supplies from the manufacturers of excipients.

Testing Facilities:

This is an essential part of the quality control, and the analytical facilities at present are not sufficient. Starting from the Central Drugs Laboratory, the Pharmacopeia Laboratory, State Drugs Control Laboratories and Independent Testing Laboratories, all need to expanded, streamlined and updated.
FINANCIAL PROJECTIONS

Introduction:

Financial Projections have been made upto the year 2000 A.D. with a view to highlight (a) the potential that exists for growth and development to meet the drug needs of the nation (b) the magnitude of the investments required; and (c) find out ways and means for financing the massive investments required to achieve this growth.

The methodology adopted for this exercise is given below:

(a) Base Year Figures

The RBI study on the finances of 1650 selected medium and large companies (published in the RBI Bulletin of September 1977) was used as the starting point. Date for the year 1975-76 published in this bulletin covers 52 drugs and pharmaceutical companies. Assuming this to be a representative sample of the industry, the data was extrapolated to the year 1978-79. A statement showing the data of these 52 companies for the year 1975-76 and the extrapolation done upto 1978-79 is at Annexure-A.

(b) Projections.

Bulk and formulations production has been forecast yearwise upto 2000-01. Projections for productions for 1982-83 and 1983-84 are available in the report of the working Group on the Drugs and Pharmaceuticals Industry set up by the Planning Commission to make projections for the plan period 1978-79 to 1982-83 and for 1983-84 (Para 9.14). Similarly, the Production of bulk drugs by 1982-83 has also been estimated in such Report (Para 9.11).

Projections have been broadly divided into blocks of 5-year periods each as they are convenient for review purposes and are in line with the Government's planning cycle. For the year 1979-80 to 1983-84, projections have been made with a view to achieve the targets set by the Working Group for the years 1982-83 and 1983-84. Thereafter, projections are also so made as to ensure that bulk drugs production would be 1/3 rd the formulations production by the year 2000. (See para 9.9 of Report of the Working Group).

Based on the projected increases in production, estimates of the incremental investments required to achieve these increases in production were made based on investment/outpu
ratios. However, as it would take some time for the investments to pick up, it was also assumed that in the initial years, the pace of investment would be slow, and that growth during these initial years would mainly come from the utilisation of hitherto unutilised capacities and productivity/technological improvements.

(c) Assumptions made

A list of main assumptions made for the purpose of above projections can be seen in Annexure-B.

Comments/Remarks:

(a) Production of bulk drugs and formulations are estimated to rise manifold (23 times for bulk drugs, and over 13 times for formulations) during the period 1978-79 to 2000-2001 A.D. To meet these production levels, massive investments of the order of over Rs. 7500 crores would be required. For this purpose, it becomes obvious that policies will have to be growth-oriented and not restrictive. A more pragmatic approach is called for from the Government.

(b) To make possible the levels of investments required to achieve the growth in the formulations output, a minimum average post-tax profit of 7.5% on the sales/output is absolutely necessary. This would mean that the ceilings on profit contained in the New Drug Policy/DPCO-1979 will have to be revised upwards. There are over 2500 units in the small scale sector (Hath Committee Report, 1975) which, in view of the uneconomic size of operations, will be having a very low level of profitability.

Hence to earn an average 7.5% return on sales for the total industry, the maximum profit ceilings will have to be raised to about 18% on sales. If this is not done, the industry will not be able to have adequate plough-back to achieve the targets set.

(c) This contention is borne out further by looking at the position is respect of bulk drugs. At the starting point (1978-79), the net worth of bulk activity was 73% of the capital employed, whereas in 2000-2001 it is as low as 52% a drop of 21%. This on uticals industry becomes a sick industry which may not be as far-fetched as it may sound.

(e) Assuming that the bureaucratic policies of the Government continue, it is questionable whether public participation in the form of contribution of additional share capital will be forthcoming.
Considering various problems involved administrative, economic etc. it is worthwhile for us to have an up to date national pharmacopoeias. When B.P. and U.S.P. are being published every 5 years an addendum every year, we can manage well enough with these pharmacopoeias which are also official under our Drug Rules. To be of value to manufacturers and control laboratories in highly industrialised countries the specifications are framed to make use of modern methods of analysis capable of speedy implementation and of being readily automated, taking care of the processes and methods of manufacture practiced in these countries. In our country of diverse climates, unfavourable heat and humidity, repeated freezing and melting in cold places, the stability of the drugs becomes a serious problem. It is a challenge to the analyst to devise simple procedures. T.L.C. would be eminently suitable, to establish identity and detect deterioration to the extent of 5% or more. If we are to be more dependent on the manufacture of basic materials in our country, and consider the economic conditions, transport problems, lack of expensively equipped laboratories, specific needs of the indigenous processes, we must have an up to date national pharmacopoeia.

How are we to achieve this objective? The present system of I.P. Committee is obviously inadequate. There has to be an independent I.P. Commission set up with a self sustaining system, adequate funds, staff and laboratory who would apply themselves to this task as it indeed is a big task. This idea is not a new one but so far has not been implemented due to reasons which are not very clear. Industry in its own interest must give more attention to this matter, individually and through associations and prevail upon the concerned authorities to set up such a commission as early as possible. This is a preferred future scenario, not by 2000 A.D. but much earlier, which all of us would like to see. Medical care in our country will get more socialised in future, increasing the number of generic drugs compared to the brands. In what way can our pharmacopoeia include more standards for the finished products which would take care of the generic drugs? This is for the future I.P. Commission to consider.

Instrumentation:

There is an increased sophistication in analytical and production technologies in the developed countries. Mention may be made of microprocessors which have revolutionised and increased the precision and accuracy of all types of procedures. These techniques will come to this country to a limited extent, mainly due to economic constraints. Even so, we may expect newer and really useful techniques like H.P.L.C., G.L.C., I.R., Mass spectrometry, Dissolution apparatus with selective mem-
branes, to become more in use as they will give rise to a greater quality assurance. There will be a demand for specialised personnel for handling of sophisticated instruments. The service facilities for the instruments, are far from satisfactory at present even in central places like Bombay. With an emphasis on the growth of the industry in the rural areas, this aspect will pose a greater problem for which we should make provisions and plans involving the instrument manufacturers. The present liberal import policy with regard to sophisticated instruments may not be there in the future and the instrument manufacturers must plan for their own manufacture. As the instrumentation facilities increase the pharmacopoeal procedures could be updated to raise the standards and promote better quality of the products.

Drugs Control Authorities

The present net result of all the quality control and G.M.P. as practiced by various manufacturers may be seen from the quarterly reports issued by the State drugs control Laboratories. Out of the samples picked up by the Inspectors from the market and the manufacturer's factories, and tested, up to 10% are declared to be substandard.
INDIGENOUS SYSTEM OF MEDICINE

In view of non availability of comprehensive figures of production and sales for the indigenous system of medicine, estimates have been made on the basis of limited available information. There are about 20 well recognised manufacturers in this system of medicine. There are likely to be more than 1200 licensed small manufacturers besides thousands of Vaidyas having their own miniature manufacturing facilities. The estimated current production is worth around Rs. 100 crores. This value is very low compared to the production of allopathic pharmaceuticals which is around Rs. 800 crores at present.

A large majority of the Indian population depend more on indigenous medicines. In terms of money value it is low but this is mainly because these remedies are low priced.

The normal trend to depend on natural remedies is increasing and even the practitioners of allopathic medicines have started searching for natural products for the treatment of their patients the world over. This is the main reason why we may expect a manifold increase in the demand for natural remedies. On the basis of estimates from the requirements of allopathic drugs of about Rs. 16,000 crores it is likely that the value of production of indigenous remedies may be around Rs. 4,000 crores in the year 2000 A.D.

This may be even more, if as envisaged in the draft five year plan 1978-83 the rural health facilities with indigenous medicine chest is fully implemented by training one community health worker for every 1000 population and the provision of 38,000 additional sub-centres for primary health, etc. There are about 700 naturally occurring independent drugs (medicinal herbs, minerals & biologicals) used in this system of medicine. Numerous formulations are derived from these drugs. Most of the combinations are pharmacopoeial and described in many old scientific books.

The Government of Bombay had appointed a Committee under the Chairmanship of Vaidya Bapalal Shah in the year 1955 and this committee identified about 40 drugs as controversial out of the total 700 drugs used. Although therefore the basic sources of indigenous remedies are limited, they permit an almost infinite number of combinations.

The important requirements to meet the growing demand for indigenous remedies are:

i) Availability of raw materials

ii) Trained technicians

iii) Adequate investment
Raw materials are likely to pose a major problem as most of these are collected from wild sources. The Central Council of Research in Indian Medicine was established in 1969, but it requires to be further strengthened to take up this job. This can be achieved if:

1. The Ministry of Agriculture in coordination with the Forest Department and the National Research Organisations can solve the problem of making the required medicinal herbs, minerals and biologicals available in abundance on a priority basis.

2. Private enterprises are given facilities and incentives for this purpose. No organised private sector company is in this field today. This would involve:

   i) relaxation of land ceiling;

   ii) income for Income Tax purpose to be treated as agricultural income;

   iii) allowance of expenses for Income Tax purpose up to 200% on these developments;

   iv) liberal financing at low interest rates for such schemes by banks, Finance Corporations, etc.; and

   v) Participation by Government bodies in joint sector schemes.

General requirements for such projects will be:

   i) experimental farms;

   ii) laboratories for testing and development;

   iii) collection and pre-treatment centres before storage of raw material;

   iv) proper packing and storing and storing conditions; and

   v) marketing organisation.

Technicians

In the indigenous system of medicine there are 112 colleges imparting knowledge and offering degrees and diplomas. We have more than 2.5 lapse practitioners (Hakims & Vaidyas). While their main profession is the treatment of patients, they also have some knowledge of manufacturing at dispensary level. However, it is essential that manufacturing at the Pharmacy level is developed intensively. We would need more technicians.

A Bachelor's degree in manufacturing and testing of these medicines should be developed to a greater extent. At present there are only a handful of institutions imparting B.Pharm. Ayurveda. This
for turning out 1000 graduates every year should be provided. Investment
Investment requirements are very difficult to assess as reliable figures of investments are not avail-
able. General incentives for the development of industries and available menas of finance also should
take care of the requirements of this industry. The indigenous drug industry should be exempted
from Government levies. such as Sales Tax, Excise, customs duty, etc. so as to keep the costs low.
This is an essential item of life just as food and water. The well-being of the population is to the
benefit of the nation's economy and progress. There fore, the indigenous system must be given
greater preference as they serve the poor and large masses of the population.
Future requirement
There are a few other points that require special attention with regard to indigenous systems of
medicine if the forecast of Rs.4000. crores or more sales by 2000 A.D. is to be achieved. These are
A) Medical & market projections

Tendency to use
1. Safer drugs.
2. Drugs of natural origin.
3. Greater understanding of traditional medicines.
5. Increased consumption of alcohol, tobacco, and other narcotic and hallucinogenic drugs.
6. Faster life - full of tension.