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The Pharmaceutical Industry: Current Challenges**

Thank you, SK. I am really honoured and happy to be here. I will first talk about Janssen Pharmaceutica. Then, I am going to say a few words about Johnson & Johnson. Finally, I will dwell on the world pharmaceutical market. How big is it? How is it dispersed? Is it fragmented? Is it concentrated? Who are the big players in the market? What are the challenges, as also the opportunities? Most importantly, the pharmaceutical industry is about health. To put it in other words, it is about life and it is about death. And that is something we are sure about when we are born—that we are going to live, and we are going to die.

Janssen Pharmaceutica was built up with the vision of one person, Dr. Paul Janssen. But it was not built up by this person alone. It was built up by a terrific team. He once said, in his own words, "I was very lucky. I was simply the conductor of an orchestra." He joined a family company. His father was a general practioner. Like a lot of companies that started out, it was easier to copy. So they copied drugs made in Hungry by a pharmaceutical company called Richter. When Dr. Janssen joined his parents' company, he was both a doctorate in Chemistry and a medical doctor. He said, "I am only going to join the company if I can set up a research lab."

That is the key for the rest of my presentation. It is all about innovation. It is all about being centred around the patient. It is not about money—it is about making a difference to people's lives. Dr. Paul Janssen was legendry. He won every award except the Nobel Prize for Medicine. He was nominated twice. Dr. James Black wrote an wonderful one-page article in the *Journal of Chemistry*, where he said that if anyone deserved the Nobel Prize for Medicine, it was Dr. Janssen. But he did not receive it because his discoveries were so many—they could not be simply described in one line. It just tells

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you what a tremendous contribution Dr. Janssen made. Today, everybody talks about globalization—we are going to do clinical research in India; we are going to do manufacturing in China; we are going to do information technology in Bangalore; we are going to do marketing in the USA. But, in the case of Janssen Pharmaceutica, it was all centred in one place to start off with; so that there was a tremendously quick feedback loop. The scientists were connected with the clinical researchers; the clinical researchers were linked to the developers for the formulation; and the developers were connected with the producers. As they developed new products, they saw the effects in human beings. Modifications, if required, were introduced by the team and not decided by committees in the United States. Decisions on the changes were all taken in the space of one location—what we call the campus environment. Very much research-driven but all in one location, which in my opinion allows for tremendous speed in decision-making.

There were many areas in which Paul Janssen made a difference. One important area is pain management and anesthesia. People can be put to sleep in two ways. One is with inhalational gases, the other is with injectables. Fentanyl is an injectable drug developed by Janssen Pharmaceutica. There is not a hospital in the world that does not use Fentanyl for anesthesia, for analgesia, for surgery. India is a region for tropical diseases; fungal infections are many. The world's leader was clearly Dr. Paul Janssen's lab in this area. Psychiatry is another area. In an earlier era, mentally disturbed people were committed to institutions. With the advent of the new anti-psychotic drugs, Dr. Janssen and his team were able to re-socialize psychotic patients, re-integrate them into their families. They could lead relatively normal lives thanks to the new treatment modalities that became available.

Janssen Pharmaceutica was acquired by a company called Johnson & Johnson. It is the fifth largest pharmaceutical company in the world. It manufactures more than pharmaceuticals. It is the largest health care company in the world, taking into account medical devices, diagnostics and consumer products. J&J is well known for its consumer brands. The company is the world leader in the baby area and among the world leaders in the skin care area. J&J is present in the anti-ageing area through Neutrogena, which is introducing a lot of new products in the marketplace today. Johnson and Johnson is a very diversified company with some very iconic brands. It is not a pure pharmaceutical company.

Today, technologies from different areas are being converged to produce products which never existed before and are going to make a tremendous

difference to people's lives. A good example is the stent. Before the advent of the stent, when a person had blocked arteries, he or she needed to undergo a bypass surgery. This procedure takes anywhere from 4 to 8 hours to complete. It is an extremely invasive, painful and traumatic kind of surgery. Now when a person has a blocked artery, they insert a very small metallic scaffold called a stent into the blocked artery. This was a tremendous advance by Johnson & Johnson. However, initially, within two years of placing the stents, the patients'arteries would again show blockages. This was because a lot of scar tissue got formed where the stent was put into the blocked artery. J&J then developed, through the convergence of two technologies, what is called a drug-eluting stent (DES). The stent is coated with a specific drug. In the old bare-metal stent, within two years, 60 per cent of the patients got re-occlusion—that is, their arteries closed up again. With the drug-eluting stent, the figure declined dramatically to 10 per cent. With a DES placed in the artery of a heart patient, he or she can go on for much longer before it needs to be replaced.

Those are the kinds of tremendous advances that are being made in medicine today. You can capture technologies in different areas of your business, bring them together and create a much newer and braver world of tomorrow. That is why this whole area of convergent technology is so very important.

I will now briefly sketch the world pharmaceutical market. The market is somewhere in the region of about US$ 700 billion. It has been growing at double digits rates for about a decade (1998–2008), at over 10 per cent. As you know, of late, health care expenditures have been rising dramatically all over the world. Just to take the United States as one market, health care is running at about 16 per cent of gross national product. Health care and the defence are the two largest components of the country's budget. Obviously, there is going to be a tremendous trend to control the growth of health care costs. Even though pharmaceuticals constitute only 10 cents of the US health care dollar, it is a very visible cost and the government will try to control it. When health care is running at about 16 per cent in the US, 12 per cent in other countries, and 6.2 per cent in India, people are going to have to control these costs. As the financial crisis continues and people have less disposable income, the growth of the pharmaceutical market has slowed down. Before the crisis, all kinds of businesses were keen to get into health care, into the pharmaceutical sector, because it was almost an assured way of making money, of being successful. Today, that is not the case. The market that was growing at 10 to 12 per cent until recently is going to grow, at best, at 2 to 3

per cent this year. Suddenly, the valuation of pharmaceutical companies has dramatically declined. Their price-earning ratios used to be in the region of 30; today it is in the range of 7–10. It is unbelievable! The other segments of Johnson & Johnson's business—consumer business, beauty care, skin and hair care—are being valued at 13. In the space of 10 years, the whole world has gone topsy-turvy.

The pharmaceutical industry has its challenges. The United States is the largest market at just under US$ 300 billion—about 44 per cent of the world market; followed by Japan and other countries in Europe. India comes at around rank 13 or 14 but will probably enter the top-10 league very shortly. Health care costs at 6.2 per cent of GNP are going to rise very quickly to 7–8 per cent. If a pharmaceutical company wants to be a global player, it has to be successful in the largest market in the world, which is the US, followed by the other markets. In this entire space, the largest company is Pfizer; J&J is number five. Among the top ten, five are US-based, five are European-based; and, believe it or not, not even one is Japanese. The geographical spread of the industry runs like this: American companies are very strong in the US. European companies are very strong in Europe, but they are also present elsewhere. Japanese companies are strong only in Japan and hardly have any presence elsewhere in the world. But that is slowly changing. Japanese pharmaceutical company Daiichi Sankyo bought a majority stake in India's Ranbaxy Laboratories in June 2009. Clearly, Japanese pharmaceutical companies are starting to nibble at the fringes of the world market.

The pharmaceutical market of US$ 700 billion is a very fragmented market. The largest company Pfizer, before it acquired rival Wyeth, has a market share of about 6 per cent, which suggests how very fragmented the market is. In individual therapeutic classes, some companies might have a 20–30 per cent share. But taking the US$ 700 billion market as a whole, the largest company has only a 6 per cent share. This explains why the market is under such pressure to consolidate—from companies who wish to increase their overall market share.

Another area of concern is declining R & D productivity. As health care gets much more expensive, the decision-makers are changing. In the past, all the pharmaceutical companies had huge sales forces, around 3,000 in the US, 2,000 in Europe, calling on doctors' offices. Today, the power of decision-making is being taken away from the medical doctor and is being shared

with the payer. This is because the payer today holds the purse strings and finds that there are limited resources available to pay for the health care bill. And last but not the least, people are shifting from expensive tertiary care to more primary care. The general practitioners, who provide such care, are called the gatekeepers. These days, before people go and see a specialist in allergy, they first consult a general practitioner, which is a cheaper way of dealing with their disease category before it gets complicated enough to go and see a specialist. So all the pressures on this industry are to reduce the bill that is being provided either to the government or to the private sector.

I will now turn to clinical trials. The trials are first carried out in rats, mice, etc. These are animal models which do not necessarily mimic human models, but they are good starters as a disease model. Then the drug is introduced in healthy volunteers, which is phase I, to see if the drug is safe in human beings before the company conducts widespread trials. Next, the company conducts phase II and III trials, where they have to prove by a statistical method that the drug works—i.e., not by chance but that it is statistically significant. A placebo might work 20 per cent of the time. But it has to be shown that the drug has a significant response, say 50, 60 or 70 per cent of the time. It might not work on everyone.

This brings us to the subject of patents. When a company develops a product, it takes a patent, which gives the company a monopoly for 20 years. Why is it important for the company to do this immediately? If it does not do so, somebody else will do it. The whole development process, including clinical trials, may take up to 10 years. Another one or two years go in getting approvals from the regulatory authority. In the drug industry, before a company can sell a product, it has to get approval, based on all the data that the company provides to regulatory authority, and show that it is effective and safe; only then can the company sell the product. So it takes a total of 12 years to bring the product to the market. The company has just 8 years in which it can recover its money and remain financially viable.

In the 1980s, the average cost of developing a new drug was about US$ 200 million, which doubled every five years. Today, the average cost is about a billion to a billion and a half dollars. Basically, the drug industry today has become a very high-risk industry. It involves huge amounts of investment with no guarantee of outcome, with a gestation period of 12 years. The other segment of the business, medical devices, presents a different picture. This segment has an average gestation period of five years with an investment of

about US$ 150 million. The medical devices industry has a price-earning (PE) valuation of 13; while the drug industry has a PE valuation of 7 to 10. Thus, the latter needs a reward which is commensurate with the higher risk.

One of the biggest issues in the pharmaceutical industry is the number of new products approved in one year in the largest market of the world, the USA. In 1997, the number was in the 40s; in 2001, it was in the 20s; for the past four years, it has been under 10. Why is this the case? There are different reasons. Cures were first developed for the low-hanging fruit—the easier to cure diseases. Today, we are looking at age- and lifestyle-related diseases, which are more difficult to cure—cancer, dementia, stroke. Cures for these diseases are harder to find and more expensive. These are the challenges facing the pharmaceutical industry.

In the case of the regulator, sometimes it pays to be risk-averse. Let me give you the example of a drug called thalidomide, sold under the name Softenon. It was prescribed to pregnant women. It had teratogenic effects. Children whose mothers had taken the drug during pregnancy were born with a limb missing. Some children had a missing arm; some had a missing leg. The drug was approved in Europe. In the United States, the regulator had not approved it. Not because they were cleverer; they were probably more cautious in getting approval. The reviewer for the US Food and Drug Administration took the research files, running into thousands of pages, put them into a drawer and locked it. She probably wanted to see how it worked in the rest of the world. By the time those kids with missing limbs were born, she still had it in her drawer. So suddenly she became a great hero. President Kennedy put a medal on her because she had not approved what was called a teratogenic drug. Not because of smartness, but because she had locked her drawer. She was using rest of the world, to put it very crudely, as a guinea pig.

In the US, when you do not approve a drug and people die, nobody says that they died because the drug was not available. There is no reward for approving a drug from the Government of United States. But there is well a reward for not approving it. The regulator approves a drug on limited data—20,000 to 30,000 patients. Then it is made available to the entire world. When used on millions of people, suddenly effects surface that were not there when the drug was used on 20,000–30,000 people. When the effects become visible, the politicians start a hearing in the Senate. The poor person who approved that drug, all with good intentions and good data, is now accused and

incarcerated by the senators who, of course, have nothing to loose. So there is a whole incentive system not to approve a drug as opposed to approve it. The opportunity cost or the hidden cost of people dying early due to non-availability of the drug is never public; you never know why they died.

Clearly, drug development is a high-risk business. But if a pharmaceutical company, in the top-10 league, manages to come up with a product that is a commercial success, it will reap rich rewards. So the problem is also an opportunity if the company is that much smarter in its research programmes than its competition.

We come back to patents, another big challenge. Of course, some of the major generic players are in India. A product loses its patent after 20 years. The cost of manufacturing a drug when a company sells it at a price of Rs. 100 is a fraction of that price. Twenty per cent of the cost has already gone into R & D. There are other costs, such as marketing, etc. The average cost of making that drug does not exceed about 20 paise in the rupee. Given the model of the generic industry, if tomorrow another company can sell the same drug, by copying the original product, for Rs. 70, it can make a very nice profit because the cost of manufacturing it is Rs. 20! (At the same time, the government is putting the squeeze on the pharmaceutical industry to reduce the cost of drugs.) Next, generic company number 2 comes on the market. They also have nothing new to offer. They too copy the original drug but sell the product for Rs. 60. So the market that was worth Rs. 100 very quickly declines to Rs. 30 because everybody is undercutting their rivals.

Once the market becomes generic, it very quickly gets eroded. Pharmaceutical companies have to be innovative. As Dr. Paul Janssen used to say, "Either you innovate, or you die", if you are in the innovation business. But, you can be creative. I will give you just one example. Risperdal, which was a Janssen drug for the treatment of schizophrenia, an anti-psychotic drug, became the largest product of Johnson & Johnson. It is selling for US$ 4 billion worldwide. When the patent goes, generic companies quickly come on the market and the same thing happens which I just described to you. However, if the company that developed the original drug shifts from an oral form to an injectable form, and instead of taking one pill a day, the patient needs just one injection a month, the company has changed the paradigm of treatment. There will much more compliance because the frequency of the dose has been reduced to once a month and the drug is still effective. The company can get a patent for a new system, a new model; and it extends the life of the

product. The company can become creative in areas which were not tapped before. In the past, the company was only focused on finding a new product. Now it can explore new models of the old product. So all kinds of creative forces and juices are coming to the top of the innovation process. The risk of the generic route also has an opportunity in terms of developing new systems. Still, the generic drug industry represents a huge challenge.

J&J is well known and studied by all the business schools. Our credo is very simple. It has got four components: Our first responsibility is to the patients, the mothers, the fathers, the doctors and the nurses. How do we get cost-effective, high-quality products to them? Our second responsibility is to the employees of our company: treat them as individuals; treat them with respect; allow them to develop their full potential. Our third responsibility is to our communities: put back into the community what we take out—in terms of the environment, the natural resources, etc. Finally, if we do all these three right, we will hopefully have a reasonable profit for the investor. When this credo was written 70 years ago, there was one investor, the founder of Johnson & Johnson. Right from those early days, the patient has been central to our whole approach to business.

The worldwide market of pharmaceuticals is US$ 700 billion. Of this, the counterfeit market, consisting of fake products, is around 5 per cent, US$ 35 billion. That is a very attractive market. It will attract the worst segments of society—the criminals, the mafia and the terrorists. These are the people who playing in the counterfeit market. The sufferers are the common citizens. When we go to the retail pharmacy to buy a product, we are scared even though it might say Dr. Reddy's, Pfizer or GlaxoSmithKline. It might not be the company or the product that we think we are buying. It might be something which could be injurious. If we are buying a lifestyle drug and the product is a fake, we are not dealing with a major a problem; it just affects our lifestyle. But if we are buying a life-saving drug and it is a fake, then it is a question of life and death and, therefore, extremely important.

The issue is not just about the pharmaceutical industry or the fake manufacturers or the counterfeiters; it is also about the public and the government. There has got to be a partnership between them and the industry. We need to create ways of identifying our product so that we know where it is located as it goes down the distribution chain to the patient. It is up to the government, the Customs, to curb the practice of manufacturing fakes and close the units immediately. Equally important, it needs to be a global effort.

Some of the fakes are being manufactured at our doorstep; the biggest producers are in China and India. Apart from being a global effort, it must be a public-private partnership. Most important, is should be a grass-roots movement because it affects each one of us. It is therefore critical that we develop systems to ensure that we have a safe supply chain in the world.

Coming to the Indian market, it is an awakening giant. If India continues to develop the way it has been, it could be a great player in an integrated global effort across the entire health care spectrum. Our country is well off in terms of skills, language abilities, cost-effective manufacturing. We signed the Intellectual Property Protection Code in 2005. The question is: Can we walk the talk? Are we able to execute patent protection? Are we able to close down counterfeit manufacturers? Are we able to provide prices that value/ reward innovation? It is my dream that India can move from a low-price generic market to a market that rewards innovation. Tomorrow, all the Indian companies will also have to innovate if they are to succeed. We cannot have a sustainable model and live out of generics. Otherwise, we will have to remain very small. My other hope is that India moves from being an exporter of generic products to becoming a major factor in the global R&D production partnership effort, which is going to give us a better health care system, a better quality of life tomorrow. I hope too that the presence of counterfeit products in India can be eliminated so that when each one of us goes to the pharmacy to buy a product, especially a life-saving product, we have a safe and effective supply chain in place. That is my wish for both India and the pharmaceutical industry and players of the world of tomorrow.

At the end of the day, the global competition in the pharmaceutical industry is going to be won by global players through innovation. That is the only sustainable model for tomorrow—for bringing down the cost of health care for each and every one, and for providing even the poorest segments of the population access to the latest developments of today and tomorrow.