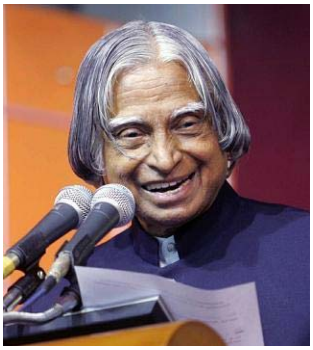

Address by the Chief Guest Dr. A.P.J. Abdul Kalam, Former President of India at the 43rd Annual General Meeting of OPPI (Organisation of Pharmaceutical Producers of India) August 8, 2009: Mumbai

Dimensions of Healthcare

"Knowledge makes you great"

I am delighted to participate in the 43rd Annual General Meeting of OPPI (Organisation of Pharmaceutical Producers of India) at Mumbai. My greetings to Pharma industry leaders, members of the government, regulatory authorities, opinion leaders, management experts and distinguished guests participating in the function. I would like to talk on the topic *"Dimensions of Healthcare".*

Pharma Vision

The global production of pharmaceuticals, branded and generics put together is of the order of $770 billion. The Indian Pharma industry at present has a turnover of US$17 billion of generics for domestic and export markets. According to the Mckinsey report, the Indian pharmaceutical market could reach US$25 billion in 2010 and US$50 billion by 2015. My visualization is; that, Indian Pharmaceutical Industry must work for getting a pharmaceutical market of US$100 billion by the year 2020. I would suggest the Pharma community assembled here to identify all missions which will make India the leader in drug production and reach this US $100 billion target before 2020. For this, our share of generic production must reach at-least US $ 50 billion and the remainder should be covered by new drugs developed by Indian Pharmaceutical Industry using their own research and development. Indian pharmaceutical companies have got the core competence for producing cost effective and quality Pharma products. Of course, the biggest mission for Pharma industry is to produce and supply quality and cost effective drugs to Indian population.

My experience with Pharma industry

I have visited number of Pharma R&D Centers. There is a great R&D effort to realize indigenous drug from indigenous molecule. In Wockhart, I found the development and marketing of three products: Biovac-B, Wepox and Wosulin are indeed competitive in the pharma market. In Nicholas Piramal research Centre, I witnessed the development of anti cancer drug, inflammation inhibitor and drug for type 2 diabetes by overcoming insulin resistance. Ranbaxy has acquired a malarial drug molecule and they are progressing towards clinical trials. International Centre for Genetic Engineering and Bio-technology in collaboration with Bharat Bio-tech is developing a vaccine for Malaria which is under toxicity trials on animals now. With Sun Pharma's experience in the field of providing healthcare solutions particularly in the area of cardiology, neurology, psychiatry and gastro enterology, the Sun Pharma Advanced Research Centre (SPARC) will have potential to design and develop molecular entities for respiratory and inflammatory disorder. The first antibody product for cancer has been indigenously developed by BIOCON in collaboration with a partner. This product is Epi-dermal Growth Factor Receptor antagonist targeting Mono-clonal Antibody. Orchid Chemicals is providing healthcare solutions particularly in the area of anti-infective therapies, cardiovascular, and neurological treatment and anti-diabetic therapies and nutra-ceuticals products. Orchids are well known for the production of antibiotic more particularly "Cephalosporins". I had also visited Alembic which is famous for antibiotic production such as penicillin, erythromycin, anti-cough & cold formulations and painkillers. Indian industry is poised to design, develop and manufacture cost effective DICOM compatible Digital X-Ray systems.

These experiences, give me the confidence that our Pharma industry is well on its way to revolutionize through the development of number of drugs needed by our country and abroad.

Contribution of Indian R&D

I have come across research and development taking place in the country in advanced field of Pharma and biotechnology leading to healthcare solutions, where R&D laboratories Pharma industries and educational institutions are partners. I would like to share with you friends.

Faster cure for TB: India has made significant contributions in developing drugs that are critically required for us. One of the achievements comes from a laboratory of the Council of Scientific and Industrial Research (CSIR). CSIR lab has developed a new therapeutic molecule for Tuberculosis. This molecule has shown the potential to cure TB in around 2 months, as against the standard treatment of 6 to 8 months. This breakthrough is very important for the researchers.

The medicine is undergoing clinical trials. I would suggest specialists particularly Pharma industry chiefs assembled here to participate in this TB treatment effort which is vital for the nation.

Typhoid Detection Kit: Typhoid Detection Kit has been developed by DRDE, Gwalior using the nano sensor developed by Prof. A.K. Sood, and his team from IISc, Bangalore. In India, the morbidity due to typhoid varies from 102 to 2219/100,000 population in different parts of the country. In some areas typhoid fever is responsible for 2-5% of all deaths.

A collaborative work has been carried out with Prof. A.K. Sood of Indian Institute of Science, Bangalore, the sensitivity of the test has been increased 30 times by applying a small electric charge (1.5 V). With this improvement, extreme low concentrations of the antigen in clinical sample can be detected. Moreover, very small quantity of clinical sample as low as 2-3 µl is required to perform the above test as compared to 10-15 micro literµl samples required for latex agglutination test.

Drug delivery system: A research group headed by Professor A. N. Maitra of the University of Delhi's Chemistry Department has developed 11 patentable technologies for improved drug delivery systems using nanoparticles. Four of these processes have been granted U.S. patents. One of the important achievements at the initial stage of drug delivery research was development of a reverse micelles based process for the synthesis of hydrogel and 'smart' hydrogel nanoparticles for encapsulating water-soluble drugs. This method enabled one to synthesize hydrogel nanoparticles of size less than 100nm diameter. This technology has been given to Dabur Research Foundation. Now I would like to present the areas needing intensive research for cancer through nanotechnology.

Research areas in Cancer Nanotechnology

Regenerative medicine: Advances in the development of nano-structured scaffolds and implants will pave way for new horizons in regenerative medicine. Development of smart drug delivery systems that can evade immunological response, target diseased parts and release the right dose of the drug can lead us closer to ideal therapeutic regimens. The drugs with such characteristics will be able to deal with effective treatment of cancer. Strategies that can provide a breakthrough in cancer therapy are:

Targeted delivery systems: Development of targeted delivery systems that will deliver the drug only to the cancer cells is an important area of research.

We have to get cost effective drugs through research. Simultaneously, the drug should avoid development of side-effects. The challenge is to identify a unique marker present or over expressed only in the cancer cells. Mostly folate receptors and epidermal growth factor receptors are popular choices as these are over-expressed manifold in cancer cells. In India, epidermal growth factor receptor antagonists (Immunotherapy/Vaccine) as Monoclonal Antibodies are produced by BIOCON. Hence a partnership between BIOCON and a nanotechnology system designer will facilitate development of cost effective delivery system to the cancer patients.

Convergence of bio-nano-info technologies can lead to the development of nano robots. Nano robots when they are injected into a patient, my expert friends say, it will diagnose and deliver the treatment exclusively in the affected area and then the nano-robot gets digested as it is a DNA based product.

High loading efficiency and stealth: Development of hyperbranched nanostructures such as dendrimers with high loading efficiency and stealth characteristics that will retard recognition by the immune system. This will enable longer circulation times for the delivery system and reduce frequent doses. The challenge here will be to strike a right balance between stealth characteristics, cellular uptake and right amount of drug release. Stealth characteristics can be incorporated by grafting polyethlylene glycol chains to the delivery systems. These are highly hydrophilic and have very fast chain dynamics and therefore retard adsorption of blood proteins. This is what has been done by Sun-Pharma. However, the cost of the drug is quite high. Further research and development are required to make the drug affordable by a common man.

Gene silencing: Use of gene silencing or RNAi therapy where specific genes that are responsible for cell proliferation and migration (metastasis) can be turned off selectively. This can lead to inhibition of the onset and spread of cancer. The challenge however is to identify an ideal site-specific delivery system for efficient encapsulation and delivery of the si-RNA (small interference RNA) to the cancer cells. This is an important area of collaborative research between Indian researchers, American researchers and medical technologists.

Imaging methods: Development of imaging methods using gold nanoparticles or fluorescent probes encapsulated in inert matrices with specific ligands that can bind to specific cancer markers. This will enable one to visualize the spread of cancer thereby enabling better diagnosis. Biocompatible probes with suitable

chemical functionalities to bind to the delivery system are the major requisites which can be achieved through the application of nanotechnology.

Selective annihilation: Another important area is Inducing hyperthermia in cancer cells using carbon nano-tubes or magnetic nanoparticles that selectively annihilate only the cancer cells on exposure to infrared radiations or magnetic field respectively. The major issue to be addressed here is the specificity of targeting, elimination of the nanoparticles and use of a suitable external trigger to induce hyperthermia. Apart from these, many new targets for destruction of cancer cells are being evaluated using bioinformatics tools. The development of a cancer database coupled with various user-specified algorithms to predict specific interactions between the potential drug molecule and the receptors on the surface of the cancer cell not only aids in lead molecule development but also to elucidate the mechanism of cell kill and cyto-toxi-city.

Innovative packaging

Spurious and Counterfeit medicines is an increasing concern for the patients, industry, and national policy-makers. It has become one of the key issues besieging the entire world - both the developing as well as the developed nations. The pharmaceutical sector is a strategic sector for India as it contributes to public health, generates positive effects on the Indian economy and improves the general level of welfare. It is crucial to bear in mind from the outset that the "pharmaceutical sector" in the broad sense includes a variety of other actors, ranging from suppliers of medicinal products ingredients (in particular the active pharmaceutical ingredient, "API"), importers, wholesalers (including parallel traders), retailers/pharmacies, and other traders (brokers, etc.). Concerning pharmaceuticals, reduced safety, quality, or efficacy can be life-threatening. In this respect, pharmaceuticals are distinct from many other consumer products.

Even one single case of spurious medicine is not acceptable because, in addition to putting patients at risk and undermining the public confidence in their medicines. The challenge is that wrongful duplication occurs in even low cost pharmaceutical products, many of which could be critical or life saving medicines. This makes it a very serious concern as such products not only harm the nation's citizens but also potentially percolate across the national borders to the entire world. Such occurrence also results into a very wrong perception of the country it originates and immensely damages the reputation of a nation as the source and hub of spurious / counterfeiting activity.

The only way to combat such a serious menace is by adopting science and technology measures. There are several science and technology measures, which have been successfully developed which are really good as well as cost effective.

These technologies can be easily integrated to provide a viable solution to the menace. Any packaged goods can use effective novel technology embedded packaging solutions which are difficult to copy yet cost effective and pose greater deterrence to the duplicator.

I have seen some company's in India who have done remarkable research and development resulting in immensely viable innovations which can be used affordably by even low cost medicines. Such innovations include technologies in material sciences as well as electronics. These innovations can be the change agent to defeat social criminals who blatantly duplicate products wrongfully, causing great harm to people at large. I had been to one such innovative company called Bilcare in December 2007. They have done some remarkable work on several technology innovations in packaging materials and have also developed a unique Nonclonable security solution which can be effectively used to not only combat counterfeit by providing a means to identify the genuinity of the medicine but also provide capability to secure the supply chain which is the weakest link attacked by the duplicator to push in spurious medicines. I was extremely happy when I unveiled the technology and had asked the group of scientists to work further on the technology to make it totally adaptable to packaged drug products. I was informed that lot of additional research has gone into the application and adaptation processes.

There is, therefore a need for much closer interactions between the pharmaceutical manufacturers and the technology providers to instigate continual innovation process and enable the incorporation of outcomes of these innovations in the form of customized solutions which in turn will provide a greater level of security and confidence to the patients. I urge the pharmaceutical industry to support such innovations happening in our country and partner for looking into implementing such innovations which will result in great value to our citizens.

The science of proteomics

India missed the great opportunity in partnering the human genome project and thereby lost the utility of right type of data. I suggest the Indian biomedical community to take the initiative to become a working partner in the proteomics project of gene characterization. Proteomics is the study of all the proteins expressed by the genome of a cell. It is the logical extension of genomics. Proteomics helps to understand the basic biological processes critical to normal cellular functions as well as the development of diseases. It identifies the essential components of these processes and exploits these components as targets in the development of new methods to prevent or treat diseases. The national programme on proteomics has to be accelerated with partnership from

industries and R & D laboratories. I would suggest that this should be pursued as a mission mode project. The proteomics resulting into a gene chip can become the future diagnosis and treatment regime for many diseases. The scientists and technologists assembled here must be aware of the progress made in the proteomics programme and understand the processes at the molecular level. This will enable genetic characterization leading to forecasting and diagnosis of the disease for adopting suitable preventive and curative measures.

Now I would like to discuss the genetic mapping of Indian population which is result of the research work of over 150 scientists.

Genetic mapping of Indian population

Indian statistical institute, Kolkatta and anthropologists from various institutes of India, and the centre for Genomic applications, Delhi has generated genetic information on over 4000 genetic markers from over 1000 biomedically important and pharmacogentically relevant genes in reference populations encompassing diversity of populations from across the country. The first phase of these results on 55 populations involving several hundred markers has been released in the April 2008 issue of journal of genetics.

This study has resulted in clear genetic profile of our populations, explicitly indicating that that there is a strong association between genetic and linguisting profiles in India and that there are significant genetic differences in the frequencies of disease – associated genetic markers. For example, this study has revealed that a known protective genetic marker against HIV-1 is virtually absent in India, implying the absence of natural or genetic protection against HIV-AIDS in our country.

The overall results of this study would help in (A) making predictions of both diseases as also the effectiveness of specific drugs used for various diseases, and (b) designing future scientific studies to understand genetic underpinnings of major diseases in India. These results have also provided the first set of insights into the processes of human adaptation to different type of environment in India.

The study reveals that the genetic landscape of Indian populations captures the genetic diversity of the world – Indian populations from a continuum of genetic spectrum bridging the two distinct HapMap populations, the Caucasians and the oriental Asians. Besides, there are populations that are unique to India mostly derived from Austro-Asiatic and Dravidian speaking studies and selecting suitable populations for testing drug efficacy. For instance, a pilot pharmacognomic study on response to sal buta mol (a Beta -2- ad renergic agonist used to treat Asthma)

identified genetic markers in a receptor gene which could classify individuals as poor and good responders – a finding that would help in better management of the disease.

It is anticipated that the Indian genome variation data along with epidemiological and associated phenotype data would help in the construction of "specific drug response/disease predisposition maps" to aid policy level decision making for drug dosage interventions and disease risk management, especially for complex as well as infectious diseases.

Dear friends, let me now focus on the international competitiveness in the Pharma sector.

International competitiveness

I notice that some our companies have been producing erythromycin for over 35 years. It is necessary to collect the clinical data from various users of erythromycin to know whether the Indian population has attained immunity against the medicine particularly the second generation users. This type of research is needed to ensure that the replacement product is planned well ahead of time to face international competitiveness. Another area where the researchers would like to work on is the development of anti-malarial drug using Artemisia annua.

Arte-misi-nin is the key plant molecule, derived from the plant Artemisia annua which is presently the most effective alternative when the malarial infection takes place due to chloro-quine resistant parasite Plas-mo-dium falci-parum. The demand of this drug is on a continuous rise and currently not even 50% of the drug demand world wide can be fulfilled mainly because of unavailability of raw material (plant herb, the source of drug molecule). Around 500 million cases of malaria are reported each year in the world and result in loss of human lives.

I would suggest our Pharma companies should become a major manufacturer of arte-misin-in derivatives using indigenous arte-misin-in available in India. Recently, a novel distinct high yielding herb with arte-misin-in genotype 'CIM-Arogya' has been developed through biotechnology approach of systematic DNA marker assisted selection at very early seedling stage from nursery itself. This genotype is the first biotech plant variety developed through molecular breeding approach and has a unique globular canopy and yields very high arte-misin-in content and herb yield. The scientists and technologists can consider large scales plantation of this 'CIM-Arogya' in the near by villages adjoining their factories.

These types of research will enable our Pharma companies to enhance its competitiveness in the national and international market. Also the patient will be coping with reduced toxicity levels of the drug.

Conclusion

Eradication of liver diseases, controlling cardiovascular diseases, Cancer, preventing spread of HIV by developing anti HIV vaccine, controlling allergy and inflammatory disorders by multiple technologies and practices and creation of competitive Pharma businesses - all need one important element, apart from other resources. That is creative leadership in health care. Who are the creative leaders? What are the qualities of a creative leader? The creative leadership is exercising the task to change the traditional role from commander to coach, from manager to mentor, from director to delegator and from one who demands respect to one who facilitates self respect. Higher the proportions of creative leaders with vision in the health care area, higher the potential for successes in research and discovery of healthcare products, leading to a healthy, and happy nation and realizing the goals of Pharma vision 2020.

I once again congratulate the scientists for their excellent work for which they have been awarded today. My best wishes to all the members of OPPI for success in their mission of facilitating the development of a competitive Pharma industry in the country. May God bless you !