

Editor's desk

Human Factor

The annual Pharma Research publication brought out by Express Pharma Pulse, this time of the year, has covered scientific topics and advances in the field during the last two years. This year, we decided to digress a bit and focus on issues other than the heavy technical aspects which are also as much relevant in creating a conducive environ for research to progress and prosper. Research is intellect and people-driven. We wanted it to be a people-focussed publication bringing out Indian research's strengths and weaknesses. The idea was to make this a light reading material, yet reflective of the various shortcomings that trouble Indian research and its administration. One must confess, this was not an easy task, especially with the cloistered thinking among some of our professionals. Research per se is confidential, but talking about research and its issues, is not. Therefore, this is one among the many negatives that need to be erased.



More than in the past, research today is a multi-disciplinary team effort requiring inputs from different areas in fundamental sciences, engineering, computing, statistics, programming and Information Technology. Managing such a divergent knowledge and skill base together with their training needs to fit into an appropriate research culture is indeed a human resource challenge to all decision makers in the pharmaceutical industry.

For example, university-industry interactions are talked about, but very little meaningful work is translating into results. We need to radically alter these equations and the government must be persuaded into giving sops to industry funding universities/research institutes so that both benefit. The Pharma and healthcare industry is witness to activities in new areas of R&D and contract research services. Ways and means to bridge the gap between education and functional needs have now to be addressed by the academia, especially in pharmacy education.

India needs practical, pro-active and positive changes in all regulatory requirements even at pre-clinical and clinical stages of drug discovery. An open regulatory system as in developed countries should be put in place without delay.

Again, the industry has not engaged the overseas Indian scientific diaspora in concrete meaningful interactions benefitting both sides. Despite the need, if a healthy transparent win-win relationship is consciously postponed, time will be running out for Indian pharma research.

Though in its infancy, Indian pharma research has all the potential to rub shoulders with the developed world. But a lot of things have to change for this to happen. A

discerning reader would find many of these in the articles, interviews and first-person accounts that are covered in the ensuing pages. As the cover suggests, the script has to change. This special issue should make everyone concerned with research to sit up and take note of the changes to be made.

A handwritten signature in black ink that reads "N.V. Ramamurthy". The signature is written in a cursive style with a horizontal line underneath the name.

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Cover Story**Miracles with molecules**

India is banking heavily on its human capital. How much can our scientists deliver? What do they need? Is creativity more important than capital? J S Sai finds out.



Quest for molecules: Can India do it? The question has been haunting the \$6 billion Indian pharmaceutical industry. India has done it in other fields in the past. "Where? When? How?" skeptics may hit back. But the fact remains that the US had got a fitting reply after it denied India a supercomputer in 1980s. "Angry does it," wrote The Washington Post after India developed Param. It happened on a much larger scale with India's Green Revolution in the 1970s, when crippling shortages scorched India's empty stomach.

Can the Indian pharma industry unveil such miracles with molecules as the World Trade Organisation's 2005 D-Day approaches? The industry, which aspires to grow to \$25 billion in the next decade, is bubbling with confidence.

Dr K Anji Reddy, chairman, Dr Reddy's Group, had said told the media that India can develop molecules at an annual expenditure of Rs 10 crore (the West spends at least \$500 million to develop a marketable molecule). After taking over as Head, R&D, Ranbaxy Laboratories Limited, Dr Rashmi Barbhैया told the media that he "plans to develop new drugs at one-fifth of what it costs in the developed countries." Besides lowering human resource expenses, he would focus on reducing the number of failures. Dr Barbhैया earlier worked with Bristol-Myers Squibb.

Do other experts in the industry agree with this? "India can make it in pharma and biotechnology," says Dr Inder Verma, professor of Genetics, Salk Institute, San Diego, California. "We have robust pharmaceutical companies like Ranbaxy and Cipla Limited, and they are already actively engaged in post WTO 2005!" Dr Prakash Amrut Mody, Chairman and Managing Director, Unichem Laboratories Limited, too is convinced that India is capable of coming out with new drugs. But how soon? "One cannot expect miracles in the near future," says Dr Mody. "Before the end of this decade, at least a couple of new drugs will see the light of day."

Endorsing this view is Dr Bala S Manian, California-based serial entrepreneur known for his contribution to companies like ReaMetrix Inc, Quantum Dot Corporation, Entigen Corporation and Biometric Imaging, Inc. "Drug discovery is a multi-disciplinary and complex science requiring a lot of scientific infrastructure to be successful," he says. "The question is not about capability or commitment but one of staying power — the process takes 10 years or more to get new drugs in the market."

**Successful NRIs**

Indian scientists have been making outstanding contributions to research in the West. If Dr Yellapragada Subba Rao excelled in the field of antibiotics (American Cyanamid Corporation) in the 1930s and 1940s, the likes of Dr Ashit K Ganguly (Schering Plough Inc) continue that tradition today. "The best estimate is that there are about 1500 professionals in industry/academics and about 1000 or so pharmacists in the US," says Utah-based Dr Dinesh C Patel, a founding partner of vSpring Capital. Dr Patel has founded several companies including TherTech, Salus Therapeutics and Ashni Naturaceuticals in the past.

Dr Bala S Manian



If our scientists can succeed in the West, why are they unable to do it in India? “One of the reasons for the success of NRIs abroad could be its ‘better’ research environment and excellent infrastructure,” says Dr Mody.

Dr Gopakumar G Nair, past president, Indian Drug Manufacturers’ Association, is quite forthright. “Where is the will, the vision and above all the passion?” he asks.

Mindset

Dr Inder Verma

Dr Nair has a point, considering the Indian pharma industry’s obsession with ‘reverse engineering.’ “We have an industry not used to investments with a long-term time horizon,” says Dr Manian. “How many times did I hear during each of my trip — how can I get a tie-up

with somebody so that I can ride on their R&D?”

But things seem to be changing with the likes Dr Reddy’s and Ranbaxy making sizeable investments for drug discovery. “The new breed of entrepreneurs in India are as good as in any place,” says Dr Verma. “They need more freedom to operate.”

Equally important is to bring about a change in the outlook of our scientific talent, reportedly being wasted in pursuit of publishing meaningless papers instead of focusing on research with huge commercial potential. “It is a rather sweeping statement,” says Dr Mody. “In any developed nation, primary importance is given to basic research. However, in an economically weak country like ours, we have to strike a balance between basic and applied research.”

“The absence of a bridge between academic research and industry is one the major shortcomings,” says Dr Manian.

How can this be corrected? “In the US, professors get a portion of the royalties received by the university from commercialisation of their ideas,” says Dr Patel. “The universities also allow professors to start their own companies. A similar system would lead to more meaningful research.”



Dr Dhananjay S Bakhle

“Indian scientists have to realise the importance of dedication, commitment and humility,” says an eminent pharma analyst. Dr Mody goes a step further. “If persons concerned are dedicated, and have clear goals, a lot more is achievable even in the present environment.”



Compromise

Knowing that discovery of molecules can bring us billions of dollars, why does India compromise on quality?

“A lot of unethical practices are happening now,” says the analyst. “Without doing a single study, some companies claim their pharmacokinetic data is ready. There are rumours that there is one set of studies for India patients and another for the West.”

Dr Dinesh C Patel

“This view may not be true of good Indian companies which maintain very high ethical standards,” says Dr Mody.

Dr Patel blasts the “attitude of making ‘fast money’ and lack of strict Government control.”

What India needs

Does India support dedicated research with the required capital and infrastructure? “As far as pharma research is concerned, it is well-known that the kind of money a leading US company spends annually on research is more than the combined annual sales of all Indian pharma companies,” says Dr Mody. “We need more infrastructure, less Government interference, better roads, reliable electricity, better transportation, less rules/ restrictions, less bureaucracy,” says Dr Verma.

Would there be any improvement in the near future? “Things may change after a decade,” says Dr Nair.

Creativity

Yet capital and infrastructure alone may not get us anywhere. To succeed, Indian scientists have to unleash their creative energies. “Indians are very creative,” says Dr Patel.

So, if Indian scientists generate blockbuster creative ideas, would money pour in? “Money follows creativity, commitment and performance,” says Dr Manian.

“If one is committed to success and has the right project, money is not an issue,” says Dr Nair. “Creativity is definitely an issue as our focus has been reverse engineering.”

Teamwork

Reorientation must happen on another front, too. “Our strength is our intellectual supremacy,” says Dr Nair. “Our weakness is the lack of team work.” “Team work is essential for success anywhere in the world,” says Dr Mody. “To translate individual excellence into practical, successful applications in industry, they need the support of persons in different fields.”

How can the desired change be brought about? “One way to solve the problem is to base bonuses on achievement of teams/ companies,” says Dr Patel. “What is frequently done here (in the US) is that a per cent of the bonus is based on achieving personal goals and a per cent is based on the team/ company achieving the goals.”

Dr Verma agrees with this. “Indians need incentives to work in teams,” he says.

Brain gain?

Several NRIs are said to be keen on moving back to India. Is this true? “I am not aware of any of my colleagues who have decided to go back to India,” says Dr Patel.

However, the fact remains that a couple of NRIs have returned home. “Look at Nicholas Piramal India Limited (Dr Somesh Sharma, the Chief Scientific Officer), Ranbaxy (Dr Barbhैया) and the like,” says Dr Manian. But their number is small. “Reversal of brain drain will happen only after 2005, when infrastructure is likely to be set up by MNCs for R&D,” says Dr Dhananjay S Bakhle, director, Medical Research & Regulatory Affairs, Aventis Pharma Ltd.

The Pfizers, the Aventis and the Glaxos may create world-class laboratories. But would the scientists be happy, considering the pathetic living conditions in India? “To be honest, most of them expect an environment (facilities and infrastructure) on par with those existing in a developed country,” says Dr Mody. In other words, they are asking for the moon. India will continue to talk big, but it is impossible to find conclusive proof of an iota of improvement in the ‘best’ of Indian cities.

So how does India convince the NRIs? “They must realise that they have to make some sacrifices if they are to succeed in India,” says Dr Mody. “Nothing can be achieved by groaning and moaning about the system (or lack of it!) prevailing here. It is for us to implement various changes that will suit our country’s needs. Further, one cannot expect things to change overnight.” What is the way out, if India has to draw big lessons from the success of NRIs and utilise their expertise? “Many NRIs are willing to help,” says Dr Verma. “They do not need to go back. There is plenty of communication by phone, Internet and travel.”

Salaries

There seems to be a huge jump in salaries in India. Some large Indian corporates reportedly hired expatriates by giving compensation packages ranging from \$250,000-\$400,000 per annum. However, are they big enough to fuel excellence? “There seems to be a big change,” says Dr Mody. “However, this alone is not enough to fuel excellence. The need of the hour for each and every company is to focus on its targeted goal with periodic reviews.”

“There is no correlation between compensation and performance at the individual level but may attract bright young people to the profession,” says Dr Manian.

“Money is an important factor,” says Dr Patel. “However, more important is the ability to grow and contribute to the success. The feeling of ownership in a project/ company is very important. From what I understand in India, the managements are too bureaucratic and authoritarian.”

Feeling of ownership! Loyalty!.. These would seem alien concepts in the absence of a good reward system that the West is known for. “No reward system exists in the country,” says Dr Mody. “Such a system needs to be reviewed periodically and changes made based on well-accepted practices prevailing in developed nations.” “The private industry is already changing this,” says Dr Verma.

HR challenges

What are the challenges before the human resources departments considering the moodiness/ ego of scientists? “Hogwash,” says Dr Manian. “There is no basis for this statement.”

“Everybody in the industry is egoistic,” says the pharma analyst. “People tend to forget that drug discovery is a multi-disciplinary effort. If one individual thinks he can create molecules by himself/ herself, he or she is mistaken. There is nothing like a chemist’s drug or biologist’s drug or a clinician’s drug. Remember that only team excellence leads to drug discovery. So people should go the extra mile to understand other disciplines. This would enrich their own contributions to a project.”

“There is no ready-made solution to the problem of moodiness/ ego of scientists,” says Dr Mody. “In any case, why are scientists being singled out? The problem exists with everyone at every level!”

So is there no way out? “We need better managers, able to harness creativity,” says Dr Verma. “We need more academic involvement in pharma/ biotech.”

Looking ahead

So India should be ready for the long haul if it is serious about molecules. “We need to get off anecdotal pontifications and focus on concrete (even if incremental) steps that can establish the framework that is appropriate in the Indian context,” says Dr Manian. “While you can think globally, you have to act locally and always strive to duplicate ‘Western conditions’ which may be relevant. Until you respect others’ intellectual property, you will never develop your own intellectual property.” “Compete with the world,” says Dr Verma. “International stature of scientists is dependent on good/ significant publication record. There is a great opportunity - and we must not miss it. It is the job of our science and technology leaders to ensure a successful transition.”

Technology leaders, are you listening?

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Interview**'Creativity, capital play a major role'**

Dr Prakash Amrut Mody, chairman and managing director, Unichem Laboratories Limited, has been actively associated with various industry associations like the Indian Pharmaceutical Association and the Indian Drugs Manufacturers' Association. A doctorate in organic chemistry, he has management qualifications from Jamnalal Bajaj Institute of Management Studies and Harvard Business School. Excerpts from an exclusive interview with J S Sai:



Several sceptics keep asking, "Can India make it?" Yet there are countless situations where India has done it. So, as the WTO 2005 deadline approaches, would India do it again with molecules?

India is certainly capable of coming out with new drugs based on original research work. However, one cannot expect any miracles in the near future. Before the end of this decade, at least a couple of new drugs will see the light of the day.

In one's quest for excellence, what is more important: creativity or MNC money? Do we lack the will to excel? Do we have enough perseverance/ determination?

I think creativity plays a major role. However, creativity alone will not be sufficient. One needs financial muscle power to successfully implement innovative ideas. In that sense, MNC money will be very useful. It is incorrect to say we lack the will to excel. Standing testimony to this are quite a few success stories in pharma as well as IT industries in India. Perseverance and determination are needed, and there is definitely a need to stress this aspect.

Several NRIs are said to be keen on moving back to India. Is this true?

It is difficult to give figures. Some people are reported to be keen on moving back.

A lot of our scientific talent is reportedly wasted in pursuit of publishing meaningless papers instead of focusing on research with huge commercial potential. How can we change this?

It is a rather sweeping statement. In any developed nation, primary importance is given to basic research. To a layman it may appear that a lot of talent is wasted in publishing meaningless papers. However, there is a clear statistical record that shows that a majority of industrial applications are as a result of fundamental work carried out in academic institutions. These may not be of any significance in the beginning.

However, in an economically weak country like ours, we have to strike a balance between basic and applied research and try to use our limited resources to our best advantage.

Interview**'Advances in research should find their way into the educational system'**

Dr Krishan Maggon, an alumnus of Delhi University and a doctorate from V Patel Chest Institute, Delhi, has been involved with post doctoral research and teaching at the University of Geneva. With more than 20 years experience in new drug R&D at reputed companies like DuPont, Bracco, Debiopharm, Cellab and several start-ups, Dr Maggon was involved in the early development of Losartan (2002 sales \$2.2 billion) and has authored over 70 research publications in various international journals.



Based in Geneva, Switzerland since 1978, he is presently an independent management consultant with a successful track record in new drug development, project management, clinical trials, business development, licensing, market introduction/support, contract and external research management. Dr Maggon who has personal experience with Indian pharma industry and has written about its R&D and clinical trial activities recently, speaks to N V Ramamurthy about his views on Indian pharma research in a forthright manner.

Even as chemistry and reverse engineering skills of Indian scientists is well acknowledged, what according to you are the newer skills this segment needs to be updated with?

The future new medicines for chronic diseases are likely to be biological like proteins, genes, cellular therapy, vaccine, monoclonal antibodies, new molecular entity (NME), so the emphasis and focus will shift from chemistry to molecular biology, molecular medicine and receptor pharmacology, from new chemical entities (NCE) to NME. Although the initial set of patents on therapeutic proteins have expired e.g. HGH, TPA, insulin, interferon, CSF, the regulatory consensus and standards for generic biopharmaceuticals may take another five years. This leaves the growth of originator biotech companies like Amgen, Biogen, Genentech, Chiron, Serono, and Novo unchallenged even after expiry of their patents. In 2002, the top selling medicine was Erythropoietin with combined sales of \$8618 million, which overtook Lipitor sales at \$7900 mn. Interferons(\$5600 mn) and insulins(\$4300 mn) made it into the top ten best selling medicines' list in 2002.

The Indian biotech products will have an uncertain period for generic biopharmaceuticals in the West. The biotech companies in India had a smooth sailing and easy approval even if the product differed from the original in amino acid composition (CSF), lack of GMP facilities, little clinical data for safety and efficacy, had a different glycosylation/activity profile and used a different non-validated expression system. Indian biotech companies are likely to remain confined to India in the near future.

For cancer, a majority of new 500 newer drugs in development selectively target cell signaling pathways, growth factors and specific proteins involved in tumour growth. Indian companies have just started copying some NCEs and preparing some analogues in the classical cytotoxic/antimetabolites like taxol, camptothecin and podophyllotoxin.

Combinatorial chemistry, receptor sub-types, nanotechnology, molecular medicine and sequencing of DNA/RNA; antisense, RNA interference, structure determination, synthesis and functions of proteins, lipids and carbohydrates; glycosylation, phosphorylation and cell signalling pathways are critical technologies for the future and are in short supply at present in India. There is a strong need for 3-4 HTS robotic screening system involving 50-60 validated targets at the same time. Similarly several functional mass spectrum coupled with HPLC and NMR are needed.

Biological skills in basic research being in early stages, how do you think the bar can be raised at academic and industry levels?

Interactions and joint research efforts of Indian research groups through ICGEB and its network of affiliates, universities/research institutions in Europe/EU and USA/Canada. Short term practical and training courses in genetic technology, proteomics, HTS robotic screening, receptor pharmacology in industry and selected research institutions on a regular basis for new trainees. The trend in the past was to go for an AID agency sponsored course, which was mainly to promote a particular country industry, mostly former Russian block. WHO or WIPO- sponsored courses in the past, in general, failed to meet FDA/EMEA requirements.

In the West, high school students in biology isolate genes, receptors and their course material is modified frequently to incorporate 2-3 years old discovery research. I first heard Nobel Prize winner Dr David Baltimore talk about the role of Caspase in apoptosis signaling pathways in 1997 at NCI/NIH, last year high school students in New York were isolating and studying the role of Caspase as part of their practical work. Universities and schools in Geneva and Switzerland continuously modify their academic course material.

The Indian schools, colleges and universities need to acquire latest instruments and technology. My last year visit to one of the university laboratory in India showed hardly any new instrument in over a decade, while several other laboratories in the capital were well equipped by European standards. Advances in research should be reflected and find their way into the educational system and research establishments.

What about our skilled Indian scientific diaspora overseas? Do you see them coming back over a period of time?

My personal contacts with university professors and researchers of Indian origin in the US, Germany, the UK, France, etc., show that a majority of professional NRI/PIO would like to have a mature win-win professional relationship with Indian institutions/industry. NRI/PIO are sick and tired of one-way flow of ideas to India without any credit in return by the Indian industry or research institutions. Only about five per cent of the NRI/PIO get some credit mostly in collaborating with Indian universities and in joint publications.

The master copier of the Indian industry has failed to give any credit, patent or rights to resulting products from ideas originating from PIO/NRI. The IP protection and enforcing the IP related arbitration or litigation in Indian courts is highly discouraging. Let EPP hear from any Indian company which respects ideas and IP of others and interested in new drug discovery, is willing to wait 5-10 years, accept initial failures and is still willing to invest in future.

Many NRI/PIO will be willing to help and organise short-term training courses on different aspects of new medicine development, provided due credit/share in IP, costs, patents and future profit sharing is agreed in an MOU and enforced under WIPO rules of arbitration under common English law. Red tape, kickbacks/bribes, changing/shifting rules and slow legal system have contributed greatly to keep off many willing NRI from returning and investing in India.

May be, you would like to mention about the conducive atmosphere, both professional and otherwise, for this to happen.

Millions of patients in India are sick, thousands are dying every day waiting for safe, effective and affordable medicines and healthcare and waiting for removal of disease burden. Every type of disease is present in India, some like malaria since the Vedic period.

The disease burden makes its contribution to reduction of lifespan and productivity. Indian patients are fed up with the election promises of politicians and inaction of health ministry officials and drug regulators to destroy and eliminate unsafe, ineffective and unapproved medicines. Indian patients are waiting for health authorities to move quickly to approve newer life saving medicines, approve more clinical trials and provide information of all ongoing and forthcoming trials and provide health insurance to all.

Indian patients are tired of excuses from the pharmaceutical industry, hospitals and medical community for their failure to provide universal quality health care and medicines at affordable prices. There is a crying need to deliver affordable quality health care and safer medicines to all needy patients. It is time that some of the Indian companies take up their moral and social responsibilities to invest some of their profits in R&D in tuberculosis, malaria, leishmania, leprosy, blindness and AIDS. Although Indian prices are lower as compared to rest of the world, they are still very high for a majority of Indian patients as the incomes levels are very low.

The Indian pharmaceutical industry developed on the "steal, copy and profit culture" and it is still the main driving factor. The same culture has been applied to the so-called new drug discovery and quickly introducing NCE/NME. Most of the companies are family based and managed and lack professional management and resources to do any effective new drug discovery. These family based concerns have a two-year short-term horizon and want to have ROI in R&D within that time-frame.

My advice to such companies has not changed since 1995 that is not to get involved in R&D and just stay in the copying side of the business. No Indian company has the resources to develop a new drug on its own or can survive a late stage product failure at phase II-III stage or market withdrawal and resulting product injury litigation.

There is a 4 per cent chance of success for development projects for new drugs in the EU/US. Only one out of four NCE/NMEs launched recovers its development cost and is profitable. The present success rate in India as believed by CEOs of Indian companies is 100 per cent. A look at the past issues of EPP will show many CEO of Indian pharma companies setting up new R&D for drug discovery and making predictions about their new discoveries in the next 6-12 months and licensing negotiations, clinical trials and marketing of their new medicines in 3-5 years.

Many of these so-called discovery compounds have moved quickly into clinical testing as predicted by the companies but without adequate safety data. Many unsafe or ineffective drugs will be cleared in the near future for marketing in India based on data generated in India. All NCE discovered in India have a straight run for clinical trial and almost automatic regulatory approval within 3-4 year, are underestimated for adverse reactions and overestimated for efficacy.

Very few of these will survive Western regulatory system or will pass regulatory review to get approval even for clinical testing in the EU/USA. Indian companies involved in the new drug discovery should learn to manage and eliminate unsafe and ineffective products and live with failure of many projects.

The new drug discovery and development should be driven by medical need and attain highest scientific, ethical and medical standards. Indian companies need to generate reliable and reproducible data for evaluation. The influence of connections, bribery and money for obtaining approvals during the new drug development is illegal and unethical anywhere in the world. The present weak, slow and closed regulatory system is a major hurdle. India will need a clean, open and transparent regulatory system like the US FDA/EMA to make a major impact.

What is your opinion on present policies, research infrastructure, attitude/mindset of Indian companies (promoters) when it comes to research and what all needs to be changed?

Compared to the situation a few years ago, there is a move for regulatory change but the process is so slow that it is almost not perceptible. Positive changes are the mandatory requirements for GMP and GCP, new GCP regulations, why there is no GLP? The Committee for Review of Drugs Regulatory System in India is composed mainly of play safe/risk averse/status quo government officials and is unlikely to recommend radical changes required to create an FDA/EMA style open system.

Several CSIR laboratories are changing their research directions and are willing to collaborate with the industry. There is absence of enforcement of current regulations due to excuses like job losses, burden on the industry, etc. An efficient regulatory system can be judged based only on results of new medicines' approval, rejections, GMP, GLP, GCP certification, inspections and removal and destruction of unsafe and unapproved products and closure of manufacturing and distribution networks.

Research infrastructure is very good to excellent in several laboratories to very poor in a majority of research institutes. The DBT model for licensing and industrial collaboration is good, efficient and seems to be working. Indian universities, research institutes, NRDC, CSIR and ICMR and DST adopt similar practices. The annual reports of DBT/CSIR/ICMR and their institutes should list the total R&D investment, royalty income as well as annual sales of the licensed products.

Providing research funding to or licensing from universities/ research institutes remains a problem because of lack of standard guidelines and IP rights to data. In the West, R&D funding can be deducted from taxes and industrial funding provides for 30-50 per cent of top university budget. Price control mechanism should be dismantled and government should negotiate deep discounts with the industry for its CGHS health scheme, essential drugs and free drug distribution for poor patients.

In the realm of contract research/custom synthesis, where is India positioned? How should management issues and problems be solved?

Around five years ago, many laboratories refused to do custom synthesis work as it was considered bucket shop type of activity or they quoted astronomically high prices. Some wanted help in opening Swiss accounts or to be paid in Switzerland only. Many laboratories wanted long-term contracts and 6 months to start the project or even offered bribes to get a project. A majority of laboratories failed to answer initial queries. The ownership, exclusivity and confidentiality of the process and data, transfer and strict adherence to timelines are still major concerns for sponsors.

Some private custom synthesis laboratories have done well and have taken away business from established CSIR laboratories and Indian pharma companies by being more flexible, and sticking to deadlines and cost control. NCI is much easier to deal with than IICT. The initial contract will be small and repeat and larger contracts will only follow if the first contract was executed within the timelines and budget. In my view, India should have secured a lion's share of global business, but has received only a fraction.

There is intense competition from China, South Korea, Taiwan, Russia, Eastern Europe, South Africa, Brazil, Argentina. This is likely to become a retail business with falling margins due to intense competition, exodus of big players and entry of small laboratories.

With respect to trained people requirement in the drug discovery process, what short term and long term strategies should be adopted and by whom?

The short-term solution is to hire trained persons from the Western pharmaceutical and biotechnology companies at international competitive salary and benefit package. The present glass ceiling of the Indian industry has to change and there are some trends in the right direction. Similarly government agencies, laboratories and regulatory bodies can rely on the NRI/PIO talent pool. A private university giving regular training courses may be the answer to long-term training.

Short term training courses in a private industry-university set up in various aspects of drug discovery and development may produce trained persons in the 5-10 year time horizon. This should cover pharmacology, drug metabolism, toxicology, histopathology, pharmacokinetics, clinical studies, formulation, stability studies, scale up and GMP production, regulatory, ICH, GLP, GCP, molecular biology and medicine, biotechnology, genes.

Finally, what is your prognosis on Indian drug discovery research?

India is just in the early phase of discovery stage. The success can come only when Indian-discovered NCE/NMEs are approved by the US FDA/EMA, and that day is far off. The highly risky international development of Indian-discovered molecules would take much longer and will result in consolidation and exit of many marginal players.

The G10 group of countries for new drugs discovery and development include the US, the UK, Germany, France, Japan, Canada, Switzerland, Sweden, Italy and the Netherlands. Of these countries, Italy, the Netherlands and Sweden have now fallen behind. Countries like Australia, South Africa, South Korea, Israel, Russia and China have failed so far to make any real impact.

India is just entering and only increased funding, persistence and learning from mistakes will pay off in the long term. I do not see any Indian discovered NCE/NME getting regulatory approval before 2010, recovering development costs or reaching blockbuster status. Of the existing development candidates in the pharma industry, one will see several terminations due to lack of efficacy, clinical and animal toxicity. This may result in shake-out and exit of weak players who got involved in new drug discovery for short-term outlicensing profits.

The Indian industry must consolidate and need several times more long-term investment in R&D to make an impact on the world stage. Doing development work in India is counter-productive under the present closed and secretive system of automatic approvals. International CROs working in India are providing good training

in GCP/ICH for clinical studies.

Indian companies have not used any international CRO for their clinical studies in India and they cannot afford to do development work in the West on their own risk. The top ten Indian pharmaceutical companies will take the ANDA route to patent expired generics in the USA/EU with little risk, relatively lower investment and good profits. In discovery research, drug delivery system CR/NDDS will be the main area of research due to lower risk of failure. The biotechnology industry in India will wait for another five years or so when agreement is reached for common standards for generic biologicals or therapeutic proteins.

To change to a US FDA/EMEA style, India requires an open, corruption-free system of checks and balances for drug approvals.

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Interview**‘Why can’t we do phase I trials?’**

Dr Swati Piramal, chief scientist and director, Nicholas Piramal India Limited, is known for her initiatives in the pharma and healthcare sectors. A post-graduate from the Harvard School of Public Health, the doctor is well known for her tech savviness. Excerpts from an exclusive interview with J S Sai:

**What according to you are the problems that need immediate attention?**

Approvals for clinical trials must be given faster. In countries like Czechoslovakia, Ireland, Poland and Singapore, you can get a clearance in 30 days. In the UK and the US, if you do not hear from the regulatory authority in 30 days, you can go ahead.

The delay happens primarily because our infrastructure is not geared for clinical trials. The Dr R A Mashelkar committee report, submitted two years ago, stressed the importance of sprucing up our infrastructure.

What are the changes that can be made to improve the regulatory system?

The problem with the regulatory system is both serious and severe. There is a dearth of trained/ experienced manpower. I had told the then US President Bill Clinton that training is one area where India and the US could cooperate. He agreed that the US FDA could train our Drug Controller General of India teams on world-class regulatory standards. But the Indian Government is yet to follow this up.

What has the Government done to increase our share in the clinical trials business?

Unfortunately, not much.

Why is the Government reluctant?

The fundamental problem is that too many ministries - health, industry, environment — are involved.

Is it true that our laws are basically geared for manufacturing?

Yes. They are also antiquated. For instance, nutraceuticals are not in the law at all. So the law is not keeping pace with technology. We still do not seem to be serious about our ethics committees. Please comment and suggest changes for improvement. In my hospital, we have two types of ethics committees - one at the hospital and the other at the national level.

Are we serious about consent forms/legalities?

I am very particular about consent forms. We have it in all languages and we make sure that everything is explained to the patient. What is more, we consider only English-speaking patients.

Wouldn't that slow down the recruitment of patients?

We have lots of patients who speak English. India is new to the clinical trials business, and we cannot afford to take any chances.

How do we tackle competition from countries like China, Taiwan, Brazil, South Korea, Russia and East Europe?

The law must be changed so that phase I trials can be done in the country. All these countries allow phase I trials. They have a stringent regulatory system to ensure that people are not exploited. There are ways to do that: ensure that your ethics committee is good, take care that the regulatory agencies have read everything, make sure that your software is world-class and that your lab is accredited. If you do all this, I see no reason why we cannot do phase I trials here.

Experts say clinical trials are considered a marketing tool to win over doctors... So, if MNCs can't launch their products in India due to the present patent laws, would they be less interested in giving us clinical trials?

Yes.

How does the marketing angle work?

As the doctors have been familiar with the drug (due to the trials), they know its efficacy, side-effects... So they would be great proponents of the drug.

So there is a commercial angle to clinical trials

No, I won't look at it that way. For, in clinical trials, you can only use a handful of doctors. In a country with 5-6 lakh doctors, you still have to convince a majority of them. May be the doctors used in the clinical trials would act like opinion leaders.

Interview

'Enhance industry's access to institutions'

Professor V S Ramamurthy started his career as researcher in Nuclear Physics at the Atomic Energy Establishment, Trombay (the present Bhabha Atomic Research Centre). He has made important contributions, both experimental and theoretical, in the areas of nuclear fission, statistical and thermodynamic properties of nuclei and medium energy heavy ion reaction mechanisms. Part of his work on Fission Theory earned him Ph D degree from Bombay University in 1971. In 1989, he moved to Institute of Physics, Bhubaneswar as Director where he initiated several experimental programmes on low energy ion beam applications and small atomic clusters. Since July 1995, Professor Ramamurthy has assumed charge as secretary to Government of India, Department of Science and Technology, New Delhi. The fellowships include those at Indian National Science Academy, New Delhi, Indian Academy of Sciences, Bangalore and National Academy of Sciences, Allahabad, among others. He has been honoured with FIE Foundation Award, 1995 for outstanding contribution in the field of Science and Technology. Prof Ramamurthy, Secretary, Department of Science and Technology, in an exclusive discussion with Jayashree Padmini talks about the three-pronged approach to take India to global levels of R&D.



Apart from a few companies and a thin NDDR pipeline, Indian pharma research is yet to grow to the international levels. Could you tell us what are the roadblocks?

It is true that in the past investments in innovative R&D has been quite low. However, now the trend is changing and the funds that go into R&D are increasing every year. It is no more just a Ranbaxy or a Dr Reddy's that enhances its R&D budget; more and more pharma companies are jumping into the R&D bandwagon with ease. But we cannot compare R&D budget of Indian companies with that of the global MNCs which have already set a track record and accumulated enough funds to divert to further R&D. This is where the government comes in. The key tasks the government looks at are establishing a strong networking among R&D institutions, setting up of research facilities, and founding testing facilities especially state-of-the-art centers to undertake various tasks for clinical trials of drugs.

Despite the much talked about talent pool and quantum of R&D being undertaken at academic institutes, results do not seem very encouraging. What are the gaps?

In fact, it is not due to the lack of research inputs but that these fail to achieve the desired level of market maturity. Hence we need to enhance industry's access to institution; this means transparency is the key word. It will also create an opportunity to convince the institutes to work on such projects that are of interest to industry. We need to nurture better equations and work out novel partnerships between industry and academia in order to utilize the potential of our scientific pool for getting more and more commercially viable R&D inputs.

What is the extent of industry academia knowledge exchange that is taking place? What proactive steps is DST taking in this regard?

The knowledge exchange is picking up now. If you see the DST programme DPRP (Drugs & Pharmaceuticals Research Programme) more than 50 per cent of the revenues came from industry. Funding combined projects by industry and institutes is one way of fostering such collaborations. We also have close interactive meetings with the industry. You can see that while we have been finalising the utilisation part of the Rs 150-crore pharmaceutical R&D fund DST have been extensively consulting the industry to draw in inputs and win their confidence.

How do you view the move of scientists to explore overseas opportunities and how will it help India when these people come back.. for eg., Ranbaxy has been on a hiring spree...

This indicates a significant factor in the movement of scientific pool that the market for trained skilled manpower has now become global. The reverse brain drain is in fact an encouraging trend as this brings in expertise with global exposure back to India. This will go a long way for India to achieve its long-term goals of

emerging as a strong innovator in R&D.

The R&D fund for pharma is yet to go operational. If you see the annual disbursement is not a very big amount in terms of R&D requirement in for drug development. Still it took years and yet we are waiting to see the results. Your comments.

The R&D fund will go operational in the coming fiscal and we expect to create capabilities in drug research. The testing facilities would act as the nodal points for industry to take its research forward with more ease. These facilities would be accessible to institutions, industry as well as individual researchers so that we could boost research at all levels. The significance of this initiative is that it reduces the requirement of investment into basic facilities by industry or individual.

Lack of infrastructure, slow movement of applications, hurdles in animal research, all have taken its toll in drug development in India. What should be approach if we want to upgrade ourselves to the global standards?

It is true that bureaucratic hurdles and lacunae have always impeded taking fast research programmes forward in the country. At DST we are streamlining procedures and taking all possible proactive steps to address these issues.

'The industry focus could be on endemic epidemiology'

Bioinformatics Society of India (Inbios) is a voluntary group set to promote Indian bioinformatics in the international arena. Inbios aims at making bioinformatics a long-term success in India and bridge the gap between the educational and corporate sector. Ashwin Sivakumar, the founder of Inbios, holds a Mastership by Research degree in Bioinformatics from Leeds University, UK, a degree in Biochemistry and an advanced diploma in information technology. Currently doing his pre-doctoral research fellowship at the Bioinformatics group at the Institute of Biotechnology, University of Helsinki, Sivakumar is keenly interested in the new and emerging IT solutions for bioinformatics research. In an exclusive interview with G Sankaranarayanan, Sivakumar shares his views on emerging bioinformatics issues and Inbios' contribution to the academia. Excerpts:



What are the objectives behind starting Inbios? How was it started and where does it stand now?

Inbios was conceptualised during a Bioinformatics Conference in Denmark (2001). I was seeing the tremendous impact a societal concept was having on this field. The International Society for Computational Biology (ISCB) has had such an impact on global bioinformatics, especially in networking the academia and the industry.

It started with a meeting of a small group of people in Bangalore. The sole aim was to help students in this field at a stage where there was such an unpredictability over the number of private centres and colleges offering the courses, etc.

We have slowly moved from a completely virtual group focussing on e-activities like e-magazine "biominds", live virtual discussions with an invited guest "biomeet", an active discussion forum at yahoo groups where we try to keep the group updated on various events we come to know, discuss research problems, ethics amongst other announcements. Our yahoo group member list currently touches 800. Now that we have slowly observed the trends in this field, we have been trying to move towards a full-fledged professional society for this field in India. Informal local chapters were initiated and we tried to do a few activities to our capacity keeping in mind various limitations.

All our efforts have paid off and we have a strong critical mass in the form of a few chapters, we have started getting known at the international level and are becoming a community by ourselves.

What are the major achievements of Inbios in India - in terms of number of programmes and other activities? How has been the response so far?

Inbios has slowly but steadily become a strong community for bioinformatics in India. We have been able to give an unbiased view on the technology to the bioinformatics community. As far as physical activities are concerned, we have learnt a lot and have been able to interact with people at different stages in their career to get to know current issues in this field.

The workshop-cum-seminars conducted in Bangalore, Chennai and Hyderabad in 2002 were a great success. The Bangalore event attracted 50 participants. The Chennai and Hyderabad events were bigger in terms of numbers and we were extremely pleased with the participation which ranged from senior scientists to students. The Hyderabad event was a very ambitious one which planned to involve both the academia and industry in a moderated discussion event open to the public. This also proposed to see presentations of work being carried out at both academia and Industry. The recognition by International Society for Computational Biology (ISCB) symbolises our growth in the years.

What do you think are the key strengths of Inbios? And what do you see are the benefits for its members?

The key strengths of Inbios are its members and the prevailing voluntary spirit. Our flexible and informal way of functioning induces a spirited contribution from the volunteers. It's due to their support Inbios has come this far with a sustained enthusiasm. Everyone is here to benefit. Such a concept is an effective way of group

learning, working as a team, knowing the science the right way and developing a spirit to contribute. The yahoo group serves as a technical forum as well as a forum to discuss other issues of the field, know about potential job announcements and events. Not to forget, Inbios is a healthy way of networking and meeting people. For me, Inbios symbolises the sincere and committed way in which Indian bioinformatics can grow.

What significant advantage does India have in bioinformatics over other countries? Can you highlight the strengths and weaknesses in terms of human resource, finance, government policies and infrastructure?

As far as advantages are concerned, I think we have a lot to contribute. There are a number of Indian origin researchers abroad contributing effectively to quality bioinformatics research and this will help a long way in inducing people to study Indian bioinformatics scenario and market. We are planning informal international chapters as well which I think might turn out to be the bridge between Indian and international bioinformatics.

The Indian IT reputation may be an important asset as well because this means that the main players from traditional Indian IT coming into this field may enjoy the confidence of similar international players. Small and medium enterprises into contract research might be able to offer competitive prices for their services when compared to other global players in the scene. In terms of profit-oriented research, the focus could be on endemic epidemiology and offering bioinformatics based insights such diseases which are region-specific.

Another area specific to India is to utilise the wealth of information available in terms of medicinal plants and ayurveda and develop informatics support for it (for instance databases). There could be international takers for such products. Indian bioinformatics is also going to develop further with the pharma industry applying more bioinformatics methodologies in their R&D.

There has been a new wave of interest among students to take up courses in bioinformatics (and biotechnology). Your comments?

Bioinformatics is heavily practical and inter-disciplinary. One, skills are only reflected by projects carried out which is also a direct reflection of the persons's skill sets. One can help himself/herself by doing some self reading, too. It's important to be net-savvy. A number of free documentations and tutorials are available on the web.

What is your take on the present status of Indian bioinformatics sector? About the present day players? Its people? Its infrastructure?

Much of the trends as far as the field is concerned have cleared up from the time of conception of Inbios. We can now see a clear set of academic and non-profit bodies doing serious research and giving quality education; a clear set of industrial players going stable and starting to compete at the world stage. Some of the labs like those at IISc, NCBS, CDFD, IMTECH, ICGEB are doing great research. We also have quality education being imparted at places like Madurai Kamaraj University, Pune University, IISc, IBAB and Anna University. Its good to see non-profit bodies like Institute of Bioinformatics (Bangalore) doing high quality research.

C-DAC is another name which comes to my mind. From the industry for instance, Strand Genomics, Ocimum Biosolutions, Ingenovis, Mascon have been doing well and are carrying out quality work and have developed a few good products. There were a few challenges, which I could think of. I would look at education as one of the major challenges. A number of private sources/companies and colleges have introduced bioinformatics courses at various levels. I am apprehensive about this trend. I am quite sure the industry providers offering short-term courses would quickly die down, especially if the education- provider has no support in terms of research.

There should be careful yardsticks for granting affiliations to colleges offering courses in this field, especially because the field is new and largely untested. One could say it's comparable to IT quite a few years back and would all level out. But the flood of private colleges offering IT related courses came after the industry was well developed and India was beginning to be one of the focal points in core IT. This balanced the ratio of production of people and employment ratio.

Bioinformatics also requires a very regular curriculum change since tools, resources and algorithms are

changing frequently - for instance the focus shift from the pre-genome to the post genome era. There are loads of databases which are going public lately. A course should thus have a flexibility of adapting to such changes so that the students are updated on the latest. So this requires highly qualified staffs who are abreast with current research.

Infrastructural challenges, of course, are that the computing facilities should be adequate with a dedicated internet connection with the latest software in use. It would augur well if all the colleges offering such courses do some research in this field. A dedicated internet connection can help bioinformatics research in a long way, especially because the number of tools and resources are available publicly. This means that moving beyond infrastructural issues, the staffs in-charge and the team offering various courses should be active in research. There should be a good number of scientific journals to access so that the students are abreast of current research.

There are many bioinformatics magazines like the Scientific Computing World/Bioinformatics Today which are given free to qualified academic researchers and staff. Such facilities should be used so that students can have a look at such magazines and get know about global scenario of bioinformatics academia and industry as far as bioinformatics is concerned. Other teaching challenges arise from the inter-disciplinary nature of the field.

It requires a flair for biology/biochemistry with strong grounding in a few aspects of information technology (databases, programming skills, operating platforms) and mathematics/statistics and, to an extent, physics. Developing practical skills is the most important aspect in this field which would come from hands-on projects under able supervision. The above points are something, which are extremely crucial when one is talking about a bachelor's degree in this field.

Industry has a major role in terms of education. They should become more pro-active by giving educative lectures on their technologies at academia. Also important is to present a realistic view of the current state of the field. A strong industry-academia collaboration is an important feature of bioinformatics scenario in the US and Europe. More efforts should be done on this front. Moving to the industry, I would also think that it will be profitable in terms of getting clients if they publish their work in reputed international journals discussing about their research and development. This will induce more interest and reliability towards the work being carried out by them. This is again a regular feature with international firms.

Interview**'VCs attract scientific talents from abroad'**

Dr Swaminathan Subramaniam is the Chief Operating Officer of Aurigene Discovery Technologies Ltd, a drug discovery company based in Boston, MA, USA with a state-of-the-art research facility in Bangalore which is promoted by Dr Reddy's Laboratories. After completing his medicine in Chennai and MD in Chandigarh, Dr Swaminathan went to the US for his PhD and worked there for four years. He came to back to India later and joined Dr Reddy's where he headed the research team for about three years. Dr Swaminathan also heads the committee for Research Services in the Association of Biotechnology Led Enterprises (ABLE). In an exclusive chat with Vijaya K, he emphasises on the role of VCs in bringing the NRI scientific community back to India. Excerpts:

**Is India attractive enough for the NRI scientific community to come back to India?**

India is probably a bigger attraction for scientists to come back because today the biotech sector is growing at a faster pace. The opportunities are more in smaller companies who can give equity and people there have the freedom to do things in innovative ways. Whereas the Indian scientific talent abroad may find it difficult in big pharma companies because of the ownership and the equity issue. In fact there are two kinds of people. The proportion of scientists who wants to come back and pursue research in companies here is still small but growing. Another set of people, typically for those who were in India, want to come back because they want to take higher responsibilities, which is not so easy in the US. Moreover, the US economy is going down now and many people are laid off.

Should this trend be encouraged?

Definitely. However, this job can be done by the VCs. They should work towards bringing back talent to India because companies grow around talent. They can be role models for existing talent in India and can grow good scientists. VCs can attract these Indian scientific talent by encouraging them to set up their own companies. But the fact is that the VCs do not look at it that way. They are more interested in hunting for business than talent. But in this case, we need to look at talent first and then business.

Do you feel that factors like infrastructure, perks, scientific culture need to be put in place while attracting talent?

These are the hygiene factors. Unless you have the right culture and infrastructure it is difficult to get talent. For a typical pharma company it is difficult to change culture but it is easier for a start-up.

How comfortable is it for a NRI scientist to work in India?

I think different people see it in different ways, particularly in cities like Bangalore it is not difficult at all. Factors like school for their children or climate may bring them back to India. In fact, today, smaller entrepreneur companies are doing quite well. This is probably because they have good culture. It depends on what kind of company he or she is working for.

Will this trend give a boost to the biotech or pharma sector?

I don't see it happening yet. Primarily, funding has to flow in and VCs have to bring back talent. We need to encourage a systematic way which makes it attractive for scientists of Indian origin working in the US or Europe to come back and set up companies here.

How successful could be pharma or biotech parks in attracting talent from abroad?

Ideas will come in and they have the opportunity to collaborate with other Indian companies. But we need a biocluster in India. Once that happens the biotech or pharma will see a self-fulfilling and promising future. We need about 10 or 20 strong companies that will grow and a good source of funding that understands the biotech sector. We need more good public limited biotech companies to make common man understand biotechnology.

Interview**'Scientific culture is getting better'**

Dr I V Sankar, currently the vice-president (R&D), Hikal Ltd, Bangalore has more than 16 years of experience in research. A science graduate from University of Kerala, Sankar joined Bhabha Atomic Research Centre as scientific officer through training School, obtained his MSc degree as part-time student from BARC and left for Australia. After his PhD degree from Flinders University of South Australia in 1984, he worked as Post Doctoral Fellow with Professor Stanley J Cristol at University of Colorado, Boulder, USA and joined as Research Scientist with Merck Sharp & Dohme in New Jersey in drug discovery programme. Dr Sankar who returned to India in 1994-1995 and joined Merind Ltd as Manager R&D, spoke to Vijaya K on his experiences in India and abroad. Excerpts:

**How comfortable is it for you to work in India after working for several years abroad?**

It has been difficult for me to get adjusted to the slow pace of work in India, however the fast developments taking place in the organisation (Merind Ltd) was quite soothing and now it is extremely comfortable for me to work in India. Here we have all the sophisticated instruments, good base of knowledge in drug discovery and passionate people to work with.

What are the major issues and concerns that come in your way in India?

The pace of the working staff, less accountability in our country and also the lack of awareness in most establishments regarding hierarchy functions is of some concern. Besides the subordinate staff are reluctant to understand the value of time, deadline and work ethics like confidentiality etc.

Are you satisfied with the infrastructure, perks and scientific culture?

Infrastructure can be improved and is getting better, perks are satisfactory as per Indian standards, scientific culture is good and is getting better.

How different is your overseas experience with the one in India?

Very different. Here I am loaded with more administrative responsibilities than scientific. Interaction with leading scientists in the new drug discovery programme is sparse or non-existent. Here we look at the possibilities of copying rather than innovation. More time is spent in molecular manipulation rather than new discoveries.

What are the main hindrances for the NRI scientific community who would like to resettle in India?

The Indian culture, bureaucracy at work place, non-acceptance of people with larger exposure to different kinds of work exposure and also the lack of professional respect and freedom are the main hindrances for the NRI community willing to work in India

What are your interests and contributions so far in research?

My interest is mainly in the pharmaceutical area, new drug discovery for cancer and diabetes. My major contribution is the development of oxomorpholin type of molecules as antidotes for adriamycin and daunomycin toxicity.

What is your vision?

My vision is to see India emerge as a leading player in pharmaceutical industry. Looking forward to Indian scientists develop block buster molecules for the treatment of tuberculosis, diabetes and cancer. To see professionals with high degree of confidentiality, work and professional ethics.

Management

With no malice towards all (including HRD)

It is important for scientists in a multidisciplinary effort to have empathy for all those around, says Dr V Sudarsanam



From the perspective of Indian research scientists in drug research, HRD always gives rise to raised eyebrows, butterflies in the stomach, as more often than not, or is it better to say that the only time it is around, it is to wind up the research division in pharmaceutical companies. Just like the generalisation in marketing “if you are not excited by a 50 per cent off sale you must be the husband,” the generalisation in the connotation of Indian research scientists is “if you are not impressed by the calibre and achievement of Indian research scientists in a pharmaceutical company, you must be (with due apologies to managing directors) a HRD person.”

Setting aside HRD for the time being, let us first look at science as viewed by scientists (as per published information) and the expectations and rewards that scientists seek.

“Divine curiosity, the researcher’s urge for creative play and inventor’s imagination - such are the fountains from which all technical progress springs,” wrote the great genius Albert Einstein.

“The explorer of nature must view research as the best of all possible sports, whose every facet - from the execution and technique to the elaboration of theory is a never ending source of indescribable satisfaction. Focus the train of thought on more and more complex associations between images based on observation and the ideas slumbering in the unconscious. Timeless value of science and the sheer joy of deciphering nature’s secrets,” wrote the father of modern neurobiology, Santiago Ramon Y Cajal in 1897.

Of course, this is not the language of HRD and it might even dismiss those as pure drivel. This is not surprising because those may not even be the language of modern day scientists, circumscribed as they are by changing values, changing landscape, changing needs and even changing circumstances.

Again, these need to be looked at in the backdrop of what scientists of yesteryears wanted. The noted biologist and grandfather of Aldous Huxley, Thomas Huxley wrote the following in his book, Administrative Nihilism in 1871- “what men of science want is only a fair day’s wages for more than a fair day’s work.”

Then there is the anecdote about Einstein at the height of his career as a Nobel laureate when he was about to join Princeton University in USA. With regard to a query as to what type of remuneration package he was expecting, Einstein had indicated that he wanted emoluments enough to live comfortably with his family to pursue his scientific interests.

However, such attitudes do not exist nowadays, nor would be wise to hold such view in the existing business climate.

During the last several decades, I had the privilege of working with and observing some fine colleagues, friends, mentors and teachers. The capabilities of some of these individuals had been something to behold. However, all of them being human, often, one comes face to face with their foibles which surface in an obvious manner, when the question of their remuneration, recognition of their work, perks, pecking order, etc arise.

The amazing thing was that with regard to many of these categories, right from the top of the ladder, all seemed to have grievances; even though each could justify their own concerns, many of them down the line felt such concerns were untenable. Amazingly when the same persons ascended the ladder to become decision makers, they made a volte face in their attitude with respect to their earlier grievances.

Here, I am reminded of some of the American presidents and actors, who in their younger years, where they were poor (by American standards) were left-wing Democrats, who when they had become rich had turned out to be right-wing Republicans.

It is probably germane now to quote here what John Haigh editor of Laboratory practice wrote in 1988

[37(11),3].

“Scientists tend to be individualistic, self-sufficient, idiosyncratic and strongly opinionated. While they respond to material rewards, they also set considerable store by the respect of their peers.” Researchers become upset if the scientist down the corridor with less experience (and less worth in their estimate) gets a larger salary increase than they do.

The other side of the picture is illustrated by the verse of Galbraith [Management Rev May 17, 1963].

*He got a fair raise; or to be precise
Just half of what he estimated
He well deserved - and only twice
What the boss believed he rated.*

These highlight the need for a balanced and realistic perspective at all levels in the hierarchy.

Biomedical research is an intrinsically slow and iterative process and even generating a promising lead molecule at the upstream end of drug discovery and optimising to a developable drug-like candidate and taking onto development is a multidisciplinary effort and multi-faceted undertaking.

Hence the contribution of one or more individuals cannot be over-rated, as without the optimal contributions of others, there cannot be any success. This adds to the problem of judging the contributions of individuals. There is also the need for scientists to accept that past achievements are past. Whether one likes it or not, one is only as good as his next important achievement. It is also important for all scientists in a multidisciplinary effort to have empathy for all those around (up, down or sideways).

For climbing the hierarchy, it is not enough for scientists to be good only in their own discipline. As a recent article in Nature highlights, “narrowness of focus is the central problem plaguing the most interdisciplinary of scientific pursuits - drug discovery. Encouraging scientists in drug discovery to step outside their own areas of expertise and chat with colleagues from down the hall to stimulate cross fertilisation of ideas will help idea generators to come to grips.”

Further, in judging performance, Indian science enormously over-rates the quantity of work. More often than not, it is the quality of science that makes the difference between success and failure.

Factors involving inter-personal relationship sometimes come to the fore in assessments, with doubts whether biases have a role in these, with the justification as quoted from an article by Dr Walter Moos, “In decision-making processes (and elsewhere) recognise that your biases may have an equal chance to be right or wrong.” I was told of a happening which covers one such situation.

In one of the research review meetings with the expert from abroad, a significant query was posed on the scientific and methodological issues in a therapeutic area to the scientist who had been working on the area for several years. The scientist who is the person who has to have the breadth of knowledge and depth of understanding, instead of clarifying the issue, cleverly side-stepped it by saying that the director is more competent to dwell on it and also indicated that the comments of the visitor from abroad will be valuable.

However, in this case every thing worked out well, as both the research director and the visitor were pretty pleased with the remark and the scientific issue was relegated to the rear, if not swept under the carpet. The scientist was one of the earliest to get promoted. It is quite possible that the scientist may have done quality work to warrant the reward or as another scientist down the corridor cattily remarked, “it may have been due to the clever human ploys on more occasions than one, or due to both.”

Again, this puts in place the need and onus on the boss to be scientifically fair and not be trammelled by extraneous considerations.

To quote Dr Moos, in most avocations, success is often the result of grit, competence and determination. Innovation (eg. breaking rules) in highly regulated activities may be punished more often than rewarded [v/s the tried and true, or, simply following rules]. The opposite is often true in research and this needs to be kept in view.

Few would disagree with the fact that a scientific career is not an easy one, but assessing research and managing researchers is probably more difficult (to bring out the best in them) so the suggestion of HR in R and D probably merits some consideration. This, however, will need a HR person with a research culture, an ability to appreciate research, vibe with researchers i.e, a person who does not start with the mindset usually prevalent in Indian management that a research division is there only to incur costs.

While talking about drugs, professor George De Stevens had said, "There is nothing like an absolutely safe drug; there never was one; there isn't one now; it is unlikely that one will be found in the future." Given the Indian experience, Indian research scientists tend to think, "there is nobody like HR person with research culture; there never was one, there isn't one, it is unlikely that there will be one in future."

I hope that the new millennium research scientists in drug discovery see corporate attitudes that make them realise that the latter statements are not true. If that happens, I can happily conclude by saying "With good-will to all (particularly HRD)."

Post-script

"In fairness, the scientific community, sometimes, is no different from the rest of the world when it comes to recognition of good performance or when accepting change. Each discovery requires the destruction of an already established idea. The more entrenched the previously held theory, the fiercer is the opposition to change.

In 1849 Dr Ignaz Semmel suggested that the most effective way to lower the extremely high mortality rate of women in childbirth was for obstetricians to wash hands before handling the patient. The medical management was unsettled by the fact that the death of so many patients could have been prevented if they had the wisdom to divine a simple fact and adopt it in practice.

In spite of the fact that never in the history of humankind has such a suggestion or idea done so much to save so many (of the women who constitute almost 50 per cent of the world's population), for this suggestion, Dr Semmel was sacked from the hospital - a very poor reflection of management's attitude which continues even today, an attitude fuelled by the arrogance of power."

The writer is Emeritus scientist, BV Patel PERD Centre, Ahmedabad

HR Training**HR challenge: Education vs. employment**

*Pharmaceutical medicine professionals have to acquire wisdom in a bitter way through the experience of making mistakes and learning, writes **Dr Arun Bhatt***

“By three methods we may learn wisdom: First, by reflection, which is noblest; second, by imitation, which is easiest; and third by experience, which is the bitterest.” - Confucius



The pharmaceutical industry has been an attractive employment option for biomedical science professionals. Over the years, there has been a paradigm shift in the industry functions from classical medico marketing and production to new areas such as research and development (R&D) and contract research services. On one hand this has increased the employment opportunities; on the other it has widened the gap between the education and functional needs. This is a new challenge for human resource (HR) managers!

New functions and skills

Traditionally, a medical adviser would manage clinical trials and regulatory affairs and provide market support. Today, with focus on quality and monitoring of clinical trials and export of drugs in countries with diverse regulations, some of these functions have become specialised, requiring different knowledge and skills. Similarly, a pharmacy professional, who was earlier involved in market support function, is now spending more time in clinical research management. The R&D personnel of yesteryears - chemists and pharmacists- were focussed on process and formulation improvements. In last few years, they have had to look at novel areas- chemistry, biotechnology, new drug delivery, patenting, bioinformatics etc. The emerging contract research organisations for clinical trials need professionals with new management skills - communication, negotiations, finance management etc.

There is a growing concern that the academic knowledge base itself is not a total reflection of the professional attributes required to perform effectively in the changing functional requirements. The challenge for HR managers is: how to get experienced professionals who have the diverse knowledge and skills to perform complex multi-skilled functions?

Functional requirements

Several surveys have highlighted the diverse functional requirements in pharmaceutical medicine.

A survey conducted by Faculty of Pharmaceutical Medicine, the UK in 1992, focussed on the training requirements in knowledge and skills area. The respondents laid emphasis on the following areas for the discipline of pharmaceutical medicine.

Basic knowledge - trial design, adverse events, ethics, therapeutics, clinical pharmacology, regulatory affairs, pharmacokinetics, statistics, pharmacology, pharmacy, toxicology, medical information, industrial issues.

New knowledge - Good Clinical Practice, study programme design, quality and audit issues, legal, information technology, epidemiology, health economics, computing skills

Personal skills - presentation, leadership, teamwork, diplomacy, training others, writing, creative thinking, conflict management, media skills Business management knowledge - decision making, project planning, crisis management, personnel management, financial management, time & stress management.

A survey conducted by Academy of Clinical Excellence (borne out of an industry - academia partnership) revealed that most participants wanted training programmes in clinical research regulations, methodology and administration. A quick glance at the above diverse areas brings out the inadequacy of knowledge and skills of a fresh medical or a fresh pharmacy professional. Most of these are hardly discussed or taught in medical or pharmacy colleges. Even the professionals, who are already on the job in pharmaceutical industry, lack a formal exposure to many of these new knowledge and skill areas.

Training requirements

The UK survey also brought to light short fall in training in some basic and new knowledge areas - ethics, industrial issues, medical information, legal affairs, information technology, epidemiology, health economics. However, the shortfall was significant in almost all areas related to personal skills and business management knowledge.

Personal skills receive little attention during the educational process, but are critical in translating an academic education into rewarding and productive work. All these subjects are hardly taught but are important to the performance of day-to-day work. For instance, when a clinical research associate monitors a clinical trial, she has to use her basic knowledge of trial methodology, GCP, therapeutic area, protocol, regulations etc.

However, when she detects a deviation, she has to use diplomacy, conflict management, and leadership skills to resolve the issue with a senior medical investigator and her superiors in the company. The training needs have to be matched with required competency levels for different jobs. The medical adviser should be fully conversant in interpersonal and management skills; whilst in some of the statistical subjects, a working knowledge may be adequate. A CRA has to be fully conversant with negotiation, time management and presentation skills.

Training and Development - A Challenge

The crucial question is - where and when can the pharmaceutical medicine professionals obtain the required training?

Most formal teaching programmes (eg., faculty of pharmaceutical medicine) cover these over several years. However, in Indian situation, the professional - medical adviser, clinical research associate, project manager, quality assurance manager - has to acquire them in a short span of time!

It is obvious that some of the training (basic and new knowledge) has to be in classroom setting. At present, we do not have any institutes along the lines of Faculty of Pharmaceutical Medicine UK to provide such training. Academy of Clinical Excellence has initiated certificate courses in GCP, Ethics, and Protocol design and has plans to develop full curriculum for a diploma course in various aspects of clinical research.

The personal skills and business management knowledge require on the job training. In most companies, such programmes are not offered to technical departments and are mostly meant for senior management. Besides, most of these programmes cover case studies from marketing angle. Such formal programmes need to be complemented by day-to-day on the job training and reinforcement from the functional head - medical director.

Unfortunately, most companies employ young medical graduates/ postgraduates as medical advisers, who lack these skills and are themselves in need of such training! There is an urgent need for human resource function to focus attention to development of these skills amongst pharmaceutical medicine professionals. Till such time, pharmaceutical medicine professionals have to acquire wisdom in a bitter way - through the experience of making mistakes and learning!

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Clinical Trials

Be clinical about trials!

To grab a major share of the clinical trials pie, India needs tough measures, writes J S Sai

The bubble of hope is getting bigger and bigger. Optimism expects India to grab a bigger share of the \$35-40 billion world clinical trials pie. Realists say that bubble would burst if India does not set her house in order soon.

But the fact remains that nearly ten years after the first global standard clinical trial was conducted in the country, India has registered phenomenal growth. From scratch to about \$100 million, according to unauthenticated data. Several Contract Research Organisations like Quintiles, Siro Clinpharm, Covance, ClinWorld, ClinInvent and ClinTec and Site Management Organisations like Neeman Medical International (Asia) have made their mark. However, India seems to be nowhere in the global clinical trials market.

Dr Swati Piramal, chief scientist & director, Nicholas Piramal India Limited, agrees that India's share at present is minuscule. "There is no accurate data," says Dr Dhananjay S Bakhle, director, Medical Research & Regulatory Affairs, Aventis Pharma Ltd. What could be the number of trials? "At present, we have less than 50 active global clinical trials in the country - even that is an overestimate," says an eminent analyst.

What could be the number of such trials in the last decade? "It would be less than 100," says the analyst. The trials cover areas like oncology, anti-infectives, neuro-psychiatry, etc. Which are the major clinical trials destinations in India? "Most studies happen in the south and the west," says the analyst.

"Vellore is the most evolved. An occasional study happens in Kolkata. Serious clinical trials are also being done in the interiors of Anand and on the outskirts of Ahmedabad." Such is the dearth of authenticated information that there is ambiguity even about the first global standard trial in India. Did it happen in 1993 or in 1995? Was it done by Pfizer or Eli Lilly?

Reasons

Experts feel that India has several advantages - small wonder some of the 50-odd CROs in the country are doing very well. But the issues seem to be even bigger. The most important one: the commercial angle of clinical trials that consume around 70 per cent of the time and money spent on developing a new drug.

"Associated with the clinical trials of a drug, doctors tend to prescribe it after its launch," says the analyst. "This happens the world over... However, if the MNCs are unable to get a decent price for their drugs in India due to the absence of IPR etc, why would they give us clinical trials? More and more commercial angles are being heaped on clinical trials."

Dr Piramal too laments, "We have not signed the required IPR documents. But India signing the WTO agreement is a way forward. However, there is still a big loophole in ensuring data exclusivity. We should immediately resolve this."

Advantages

India is said to have several advantages in clinical trials: low R&D costs, large pool of treatment-naive patients, speed of recruitment of patients, good medical infrastructure, high standards of intellectual capital who are fluent in English. The last one is a major advantage as clinical trials need extensive documentation.

"In India, clinical trials can be done at about one-fourth cost as compared to the West," says Dr Shoibal Mukherjee, senior director, Pfizer Limited. "But that is not a primary consideration for the West as the volume of work coming to India is at present insignificant."

Guinea pigs?

As for volunteers and real patients, there seems to be an acute shortage in the developed countries. India has every conceivable patient/disease. But there are allegations that Indians are being used as guinea pigs —

“People are not seeing this in the right perspective,” says Dr Bakhle. “At present, most of the patients come from the US and Europe. But now, as trials are happening in India too, people are saying that Indians are. This is incorrect. Doesn’t India and Indians too have a responsibility of partaking in the drug development process?”

Dr Chetan Tamhankar, general manager, Siro Clinpharm Private Limited, agrees that clinical trials bring Indian patients tremendous benefits as they get access to the very latest and possibly the best in treatment.

Quality

The quality of work done in India has improved over the years. However, India is still not able to meet the US FDA’s requirements fully. “If they do an audit, maybe we would meet 60 per cent of their requirements,” says Dr Tamhankar. “Integrity is another issue,” says the analyst. “Do you know that the same patient is enrolled in several trials? I am not referring to an isolated case. However, India has countless good investigators who do not come into the limelight because of their poor marketing skills.” How true are the allegations of fudging? “Yes, there is tremendous scope for fudging because I cannot go to places like Muzzafarpur without informing the investigators,” says the analyst. “For, there are no hotels in such places. When they know I am coming on a particular day, they may stage-manage everything.”

“Unless there is an audit, fudging may go undetected,” says Dr Arun Bhatt, president, ClinInvent Research India Private Limited. “But in the case of global trials, the chances of fudging are remote due to stringent audits.”

“There are so many checks and cross-checks in the process of Good Clinical Practice (GCP) trials that it is very difficult to fudge or resort to fraud,” says Dr Tamhankar. “We are using the US FDA-approved software NuGenesis,” says Dr Piramal. “It eliminates the chances of fudging completely. If you do a test, it is automatically reflected in the data. Unfortunately, fudging might be happening with small CROs.” Whose responsibility is it to hire dependable investigators who are familiar with ICH (International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use) and guard against fudging? “The sponsor’s,” says Dr Mukherjee.

Ethics

“Most Indian hospitals do not have ethics committees,” says Dr Mukherjee. “Even if they are there, they are not properly constituted. The committees do not have standard operating procedures. They do not meet frequently — some of them meet once a year.” “Ethics committees have to be independent,” says Dr Bhatt. “How can this be achieved if the hospital chairman/director heads the committee?” When is India likely to see a significant jump in the number of institutions having world-class ethics committees? “This will happen only when more clinical trials come to India,” says Dr Bakhle.

Consent forms

Are norms being followed with regard to consent forms etc? “By and large, these are being adhered to, thanks to the hue and cry over the two recent controversies,” says Dr Bakhle.

“Getting informed consent in this country is difficult because of high illiteracy levels,” says the analyst. “How does one explain complicated medical concepts in Hindi when they are no equivalents? Even if one does, it might scare people unnecessarily.” “International consent norms are followed by investigators,” says Dr Mukherjee. “But this does not mean all studies are done to that quality. Quality may suffer in the case of local studies.”

Regulation

Is it because our regulatory system is weak? So antiquated are our laws that they still insist on trailing the West in clinical trials to protect Indian patients. The law still does not allow Phase I studies. “There have been significant changes in the regulatory system, but we have miles to go,” says Dr Tamhankar. “It still takes six months to get the clearance for a clinical trial. In the US, however, you are free to start your trials 30 days after you submit your papers. In case it has any reservations, the FDA seeks clarifications.”

“The delay happens primarily because our infrastructure is not geared for clinical trials,” says Dr Piramal. “The Dr R A Mashelkar committee report, submitted two years ago, stressed the importance of sprucing up our infrastructure.” “The Drug Controller General of India Ashwini Kumar is doing a good job despite inadequate staff,” says the analyst.

Dearth of professionals

Despite the hype about clinical trials, the number of GCP-trained investigators in India is very low - about 200, according to a report. “Clinical trials are not part of any hospital’s main interest,” says Dr Bhatt. “Most doctors would like to be practitioners. Few want to be researchers. This is true the world over, and more so in India as clinical research is yet to be considered a career.” “Such trials are still considered a research activity that is at best an additional source of income,” says Dr Bakhle. There are rumours that some Indian doctors see too many hassles in clinical research - for instance, the ethical issues. “Unlike in foreign countries, doctors associated with Government hospitals in India cannot seek a personal grant for doing such work,” says an expert. “But slowly things are changing.”

Training, education

What could be the right qualifications for an investigator? “This depends on the therapeutic area, the complexity of the trial and how common (or rare) the disease is,” says the analyst. “At Wellquest, we hire MDs in clinical pharmacology,” says Dr Piramal. “Unfortunately, our medical colleges produce only 20-30 of them annually.”

India needs thousands of professionals to grab a bigger share of the clinical trial business. Is enough being done to train professionals? “Barring exceptions like Academy for Clinical Excellence (a Bombay College of Pharmacy and Pfizer initiative), there is no broad-based training available,” says Dr Tamhankar. “Universities should consider changes in curriculum.”

What could be an investigator’s profile? “An investigator should have a scientific bend of mind, treat GCP guidelines as sacrosanct and exercise tight control over the project,” says Dr Bakhle. “He has to be familiar with adverse-event monitoring techniques and has to be alert so that any new development is promptly detected. He has to be well-versed with regulatory norms.” Do sponsors prefer senior or junior doctors? “You have a very young community of investigators which is very attractive,” says an eminent clinical trials expert. “However, the fact remains that experienced clinicians who have reoriented themselves, are a big asset.”

MNC requirements

What does the West look for? “Time is the essence in such studies,” says Dr Tamhankar. “Recent estimates show that a year’s delay in launching a new molecule could cost a pharma company \$ 390 million. It might lose the opportunity of being the first to hit the market.”

So why are we not able to offer these services? Besides the above-mentioned reasons, there is increasing competition from other countries like China, Taiwan, Brazil, South Korea, Russia and East Europe. “There would be serious competition from Brazil and South Korea as they recognise patents,” says the analyst. “The question of competing with other countries is not very critical,” says Dr Gautam Daftary, managing director, Siro Clinpharm Private Limited. “The West already has several compelling reasons to choose India. Any new drug that will be developed in future ought to be tested on Indian patients.”

Documentation

Documentation in Indian hospitals is not really up to the mark. “However, there are exceptions like Amrutha in Kochi, where all the documentation is online,” says Dr Mukherjee. “So hospitals have to be better wired. We need better documentation norms.” “Our hospitals should build up their databases so that they need not grope for patients when a project comes up,” says Dr Bhatt. “They have to improve their patients’ records.”

Future

“According to McKinsey, India’s pie could be \$1 billion in 2010 (by then, global spending is expected to grow to \$ 70-90 billion),” says Dr Tamhankar. Many experts agree with this projection. But when even a speck of

doubt is enough to ruin reputations and endanger lives, would any one consider India for a bigger share? For, India is now able to meet only “70 per cent” of the international requirements. Comply with their norms fully, and the bubble of hope would turn India into a global clinical trials player! That seems to be drug MNCs’ message!

Policy**Will the benefits of science reach all of society?**

*Absence of an equitable sharing will lead to increase in the already widespread inequities in health, wealth and education, says **Dr David J Triggle***



Dr David J Triggle is a professor in the School of Pharmacy and Pharmaceutical Sciences at the State University of New York and has received several prestigious awards. He has served in a variety of capacities in several universities in the Middle-East, China and India. The Economist of January 3rd 2002 contained the following observation:

“That the mental landscape today is almost unrecognisable from that of, say two centuries ago, is due entirely to the work of two groups of thinkers: scientists and economists. Add engineers to that list and you have an explanation for why the physical, commercial, and political landscapes have changed just as radically.”

But it is not all of science that has contributed so significantly. It was the British physicist and Nobel laureate Lord Rutherford who so famously observed that, “In science, there is only physics, all else is stamp collecting.” And the great industrial revolutions of the 18th and 19th century were based upon the great discoveries of physics that ultimately transformed the 20th century bringing with them all of our mechanical discoveries from steam engines through sewing machines, the internal combustion engine to nuclear fission.

Appropriately enough it is also physicists who have helped transform biology from a qualitative descriptive entity into a dominantly quantitative discipline deriving its power from the information base of the genome. Indeed, one may argue with some confidence that just as the 20th century was dominated by the great discoveries of physics so will science of the 21st century be dominated by the paradigms of biology.

These paradigms that govern biological behaviour, the genomic-based themes of — diversity, replication, evolution and self-organisation — are increasingly being realised as generally applicable in disciplines outside of biology from chemistry to engineering and nanotechnology - disciplines that are an integral component of the new pharmaceutical sciences. These four themes are linked intimately through the process of biological recognition - those molecular interactions that determine the oft exquisite specificity of recognition that is so common in biological systems and that we seek to emulate in our approaches to medicines discovery in the 21st century.

It is perhaps not too much to anticipate that this century will see the realisation of Paul Ehrlich’s goal of the “magic bullet” — the drug targeted with complete specificity and selectivity to the disease target. Few will argue that we cannot achieve this goal and that the future of human health benefits should not be one of increasing promise.

Newborn children will start life with their genes already profiled and their health risks quantitated, ‘personalised’ medicines will be the norm through pharmacogenomics, gene and stem cell therapy will have come of age with major impact on degenerative disorders and injuries, and human cloning will be a reality. This new world will be one of artificial cells and machines with many being specifically created with an expanded genetic code to perform specific tasks.

However, the impact of the paradigms of biology will not be merely on our technologies. There will be a major impact on our science disciplines, the ways in which science education occurs and the organisation of scientific research. The early 20th century concept of scientific disciplines being neatly housed within their own carefully delineated boundaries, where the high priests and practitioners are carefully credentialed primarily for their own disciplinary benefit, and communicating only exceptionally has been under increasing pressure for some time.

This pressure will increase with the realisation that our understanding of the life process requires the simultaneous application of and integration of a multiplicity of formerly independent disciplines from chemistry and computing through electronics and engineering to genetics and geography - no less, in fact, than a “systems approach” to biology that recognises that a complete understanding of the organisation and signaling networks of living cells will not come from a single disciplinary and reductionist approach.

Finally, the organisation of biomedical research needs a significant rethinking. Some of this has already occurred with, for example, the large-scale human genome project. However, as outlined in a recent report from the National Academy of Sciences of the USA ('Large-scale Biomedical Research. Exploring strategies for future research,' National Academy Press, 2003; www.nap.edu), the need to more effectively define national priorities, to have effective management, to recruit and retain scientists capable of working in highly interdisciplinary and rapidly moving environments, the need to examine carefully the impact of intellectual property protection on scientific creativity are important challenges to national science policy in both the rich and the poor worlds.

The recent communication from the Commission of the European Communities on life sciences and technology (<http://europa.eu.int/comm/biotechnology/pdf/doc—en.pdf>; Brussels, 2003) has also stressed the need for greater integration and less fragmentation of research across borders. These advances in science also bring powerful public policy issues in two principal areas. First, the ethical issues arising from our increasing command of, and power over our own genome - genetic privacy, stem cell use, cloning, artificial reproduction, etc. These issues require intelligent and broadly shared public discussion and cannot be obscured under a cloak of fundamentalist dogma.

Even a rich country such as the United States has thus far failed in this respect because of widespread and irrational fundamentalist beliefs. Second, and of even greater importance is the issue of the sharing of the benefits of science. In the absence of equitable sharing, the already widespread inequities in health, wealth and education will continue to increase.

The latest report from The United Nations Development Programme - "Human Development Report: 2003" (www.undp.org) noted the following for the year 2001:

- 54/175 countries are poorer than in 1990
- 21/175 countries have more people starving than in 1990
- 14/175 countries have higher infant mortality than in 1990
- 12/175 countries have less primary education.

This is naught for our comfort. Breaking this cycle is less a matter of science than it is of education and public policy. Absent significant change the promise of science as the greatest rational achievement of mankind will not be realised in the 21st century for a major fraction of the world's population. This failure will impact both the rich world and the poor world through increased political, environmental and infrastructural instability.

For the poor world, the major and decisive question is to what extent the economic policies of the rich world have impacted, positively or negatively, their own development. Certainly in the areas of medicines delivery and development the rich world has attended almost exclusively to its own priorities.

The profit- and market-driven model of drug development does not work for the poor world. Hence alternatives such as that launched by Medicines sans Frontières of the Drugs for Neglected Diseases initiatives (www.accessmedmsf.org/dndi/asp) that is a model of a needs-based, as opposed to a profit-based, initiative are to be welcomed and should be examined very carefully in the developing world.

India has the opportunity to play a major role in medicines development in the 21st century. It has an existing generic-based drug industry with an increasing focus on discovery. Second, there is a large and talented pool of scientists both in India and abroad; many of the latter are likely to express interest in return as the scientific infrastructure in India improves (much as is happening in China). Third, information technology, an increasing important component of scientific disciplines, is already world-class in India. Fourth, India already has a significant advantage with the widespread fluency in English. Fifth, India is home to a vast store of "indigenous" pharmaceutical knowledge derived from its traditional medicine. These medicines contain molecules 'forged in the crucibles of evolution' and that will provide new molecular structures for development. Finally, it is quite clear that the increasingly large size of the multinational pharmaceutical companies has not endowed them with creativity that scales to size: hence, the inability to compete on the same financial basis or personnel scale is not an automatic disadvantage.

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Nostalgia

Pioneering snake project

*Centre for Cellular and Molecular Biology Director **Dr Lalji Singh** reminisces his early days in snake research at Institute of Animal Genetics, University of Edinburgh, which led to a great scientific discovery*



My fascination with genetics began while specialising during my post-graduate studies. I started working on the Cytogenetic studies of snakes since my MSc final year in 1966. The study on snakes (the first of its kind in the world) was my special paper in MSc final year carried out under the supervision of the then Professor and Head of the Department of Zoology, Benares Hindu University, Prof. S P Ray Chaudhuri, a famous geneticist.

During my MSc final year, I did karyotype analysis (chromosome analysis) of both sexes of three species of snakes, which accidentally happened to belong to three different families representing different evolutionary status. We discovered that in the primitive species of python (Amar), belonging to the primitive family Boidae, both the sexes had identical chromosomes.

Unlike the highly evolved species of vertebrates, including humans, which have a sex-determining chromosome Y in the male not present in the female (XY/XX), the sex determining chromosomes in this primitive snake were unidentifiable. In the highly poisonous species of snake cobra, belonging to the highly evolved family Elapidae, however, a chromosome was found exclusively in the female, which was not present in the male. Unlike the Y chromosome of human, which is confined only in the males, this chromosome was confined only in the females.

We, therefore, designated it as the female determining chromosome W in order to distinguish it from the Y of human and described this system of sex-determination as (ZZ/ ZW). The third species of non-poisonous rat snakes representing an intermediate state of evolution showed identical chromosomes, in both the sexes like the primitive python. But now, by using DNA probes developed by us, it is possible to identify the female-determining W sex chromosome in this species indicating the intermediate state of differentiation of sex chromosomes. These observations made us realise that the snakes are the only living species of vertebrates today which have preserved the evolutionary accident representing various states of differentiation of sex chromosomes in a remarkable manner.

We could realise the potential of using snake as a model system for understanding the molecular basis of what makes a man a man and a woman a woman. The Y chromosome represents the end product of the evolution of sex chromosomes. In 1974 when I was offered the Commonwealth Fellowship, I had a problem of placement because I wanted to work on snakes at the molecular level for which facilities were not available in India.

There was no one in the world working on snakes at the molecular level. Dr K W Jones of Institute of Animal Genetics, University of Edinburgh agreed to allow me to work in his laboratory for nine months, provided I worked on his research problem. He was then working on a class of repetitive DNA in primates including human. He was internationally renowned for his work. I, however, refused to work on his project. I wrote to him in detail about my research on snake material. In my initial proposal, I predicted the existence of sex specific repetitive as well as unique DNA which would be W chromosome-specific in snakes. It would be possible to separate this DNA from the rest of the genomic DNA only in snakes.

My prediction was based on certain characteristic features of the W chromosome, which was very different from all other chromosomes. Since I was carrying my own money, Dr Jones finally agreed to let me work in his laboratory on snakes. He, however, made it clear to me in writing not to expect guidance from him on this project, as he himself has no experience of working on snakes. Dr Jones also warned me that I would have to arrange for snakes myself.

I finally joined his laboratory on 22nd September 1974 for nine months. It was very frustrating in the beginning for me because I could not get any live snakes in the UK. Finally, Prof Chaudhuri, succeeded in getting the

permission of the Indian Ministry of Education to send 50 live poisonous snakes (Cobras and Kraits) to me to Edinburgh by an air-mail consignment. He even paid the airfreight from the contingency grant he had for his own research work in Calcutta University. I received the consignment. When I brought the consignment to the lab, all scientists and technicians except Dr Jones left the laboratory.

He, however, could not hide his fear. I kept the snakes in my room in the lab in Edinburgh for several months. That was the beginning of my work. When for the first time by using biochemical means and analytical isopycnic gradient centrifugation we detected sex difference in snakes at DNA level, I was highly excited. Dr Jones, however, did not believe it. It took me another six months to isolate that DNA and demonstrate beyond any doubt that, that DNA is exclusively present in the W chromosome which is confined to the female sex.

I remember it was a midnight when I developed in situ hybridised slides, stained them and placed it under the microscope. I found that the female specific DNA, which I had purified, has hybridised exclusively to the W sex chromosome of snakes. This was the ultimate proof. I phoned Dr Jones and told him about the result. He immediately came to the lab and saw it under the microscope. From that day, snakes became a major project of his laboratory. He told me then that until that day, he was not convinced about the feasibility or even the objective of my snake project. He had agreed to take me simply because he was not investing anything in it, excepting the space he was providing, because I was sponsored by the Commonwealth Fellowship.

My Commonwealth postdoctoral fellowship was originally for nine months. Based on the progress I had made during this period, as an exceptional case, I was given an extension of 14 months. However, before I could complete the duration, my passport was taken back and I was forced to return to India. This was done because in 1974 I was awarded Indian National Science Academy medal for Young Scientists for my outstanding contribution in the field of science.

In 1976, Mrs Indira Gandhi's government decided to stop the brain drain by forcing the scientists, who were honoured with national awards, to return to India. In 1976 I returned to my home village without any job. Dr Jones wrote several letters to the Indian High Commission in London and to the Indian Ministry of Education in this regard but with no effect. He, however, promised to keep on sending my salary to India until we succeeded in getting permission for my return to the UK. He asked me not to accept any job here. He informed the administration of the Edinburgh University that I had gone to India for collecting snakes and that my salary should be directly sent to me.

Within a week of my arrival at my home village at Jaunpur district, I got a letter from the Ministry saying that I was now on duty and that I could not leave the country for the next 3 years. I was surprised because I had no job. I wrote to the Ministry regarding my appointment and the nature of my duties. Within two weeks, I got an offer from CSIR appointing me as a Pool Officer in any institution in India. I refused to take up the temporary position.

After this, the Ministry stated that I was offered the poolship by CSIR but I refused to join it. Within a few days I got an urgent letter from the passport officer, Calcutta, who had issued my passport, ordering me to surrender my passport immediately. I went there and handed over the passport to the passport officer. He impounded my passport and refused to renew it without giving any reason. I started working with Prof S P Ray Chaudhuri as a guest scientist.

Later Prof Ray-Chaudhuri and Prof A K Sharma, the then Head of Botany Department of the Calcutta University wrote to the Ministry to allow me to return to Edinburgh to complete the important research work I was doing before I came back to India. They convinced the ministry that my work would bring glory to our country. Dr Jones also wrote to the Ministry.

After six months, I was called for an interview by the Ministry. They forced me to sign a bond that I would complete my work there in three years and return. Prof Mohan Ram of Botany Department, Delhi University helped me finally in getting the permission of the Ministry to go to Britain. I finally returned to Edinburgh again after spending six months in India without any job. I shall never forget the help which Dr Jones and Edinburgh University provided me when I spent six months in India without any employment.

After Emergency, three years passed, but nobody bothered about my return to India. I started feeling bad that earlier at least the Government of India felt my absence, but now nobody cared. I finally returned to India to accept the offer made by the then Director of CCMB, Dr Bhargava, in 1987. I have no regrets so far. Initially,

when Dr Bhargava offered me a position in CCMB, I put about 20 to 25 conditions to him. I decided to join CCMB only after Dr Bhargava showed me the facilities there and told me that the entire lab was at my disposal. By then Dr Bhargava had kept the position vacant for me for four years. The facilities were on par with that of research institutions in the United States and other countries.

It was our snake study, which revealed to the scientific world for the first time that the Y chromosome is strongly sex determining. It also revealed that the entire Y chromosome is not necessary. Only a very tiny part of the Y chromosome if transferred to the X chromosome is necessary and sufficient to convert a female mouse into a male.

This finding was published in the most prestigious international journal Cell. This was entirely based on snake DNA. This finding was highlighted in News and Views in Nature several times. It was also highlighted in New Scientist.

This study became the model of understanding the basis of sex reversal in human. Now the probe, which we have developed, for DNA fingerprinting is the outcome of our main project on molecular basis of sex-determination. Along with my colleagues, I developed a probe called BKM-derived probe for DNA fingerprinting as a consequence of my internationally well-known work on the mechanisms of sex determination. This indigenously developed probe is presently being extensively used in forensic investigations, paternity determination and seed stock verifications.

DNA fingerprinting evidence was presented in the court and for the first time in the annals of Indian history this result was accepted as an infallible evidence in the court of law. It is my most cherished moment though I went through a harrowing experience of making the rounds of the court to present my case. Since then, this technology has been used in more than 500 cases of paternity disputes and identification of missing children and mutilated bodies. These include the sensational assassination of former Prime Minister Rajiv Gandhi and Swami Premananda case.

At the helm of affairs of the CCMB, I was able to develop the centre to international standards. I have never regretted my return to India. The government has been positive and responsive to all the requirements of the CCMB. My approach has always been to practically demonstrate to the government the feasibility and viability of and the need for launching various projects and departments.

So, I do not endorse the view that the government is indifferent and disinterested to your proposals. Abroad, we are always treated as second class citizens, irrespective of our talent and knowledge. Here in India, my work has been greatly appreciated. Irrespective of material benefits, this is what I felt was a befitting recognition of my work.

(As narrated to Satyapal Menon in Hyderabad)

Education

More research scholars would be needed after '05



Dr (Prof) A K Bandyopadhyay, head, Department of Pharmaceutical Technology, Jadavpur University, Kolkata, speaks to Joy Roy Choudhury about the issues and challenges faced by pharmacy colleges and other educational institutes in breeding world-class talent here

On lack of meritorious students

See, I think there are three issues, which the pharmacy colleges and other educational institutes in the country face in breeding world-class talent. First, obviously is the student. Until and unless meritorious students come to pharmacy colleges we won't be able to breed world-class talent in the country.

But, fortunately, more and more students are now coming into this profession. Advancement of technology has opened up new vistas of opportunities for these students. More than 200-odd private and government pharmacy colleges in the country are producing world-class talent who are making India proud in the international arena. But a student should keep in mind that he has to work very hard to excel in this field.

Students who want to make a quick buck would be disappointed. They have to stick to their objectives. I sincerely believe that after the products-patent regime comes into effect in 2005, the country would need more scientists and research scholars.

They have to concentrate on research activities for the welfare of the masses. They may have to wait for years for achieving the results. So, more and more good and meritorious students should come into this sector. As a member of the AICTE inspection team, I have visited several pharmacy colleges and institutes in the country.

On lack of proper infrastructure

I think the second most important issue faced by the pharmacy colleges and institutes is the lack of proper infrastructure. Very often, we find out that the laboratories of pharmacy colleges are ill-equipped and, in some cases, expensive instruments are kept idle. A state-of-the-art laboratory is essential to breed international talent. Gone are the days of theoretical classes when a professor used to teach the students with a chalk and a duster. Until and unless the students get to have a feel of the drug manufacturing process, the industry would not absorb him. He should be abreast of the latest technological advances. To breed international talent, the pharmacy colleges in the country, whether private or government, have to invest in their laboratories. We, at the Department of Pharmaceutical Technology, Jadavpur University, have a state-of-the-art laboratory to facilitate the training of the students.

The laboratories should be equipped with instruments like HPLC, HPTLC, Nucleic Acid Sequencer, Protein Sequencer and host of such equipment. The students should have online and offline access to the latest journals and books on pharmacy and pharmaceutical technology. The infrastructure and laboratories in many pharmacy colleges of the country are below par.

This, I think is a major impediment towards breeding world-class talent. In this case, I think the ex-students of the respective pharmacy colleges would be of much help. The respective institutes can approach their former students to help their alma mater in procuring these sophisticated equipments.

Recently, an alumnus of the Jadavpur University, Dr V Ravi Chandran, who has been associated with several multinational pharma companies in the US and has made his mark in the global pharmaceutical map, has donated a sum of Rs 53 lakh to the Department. When asked, what should be done to bring back these talents into the country, he said, its for sure that majority of them would not like to return back to the country as very few Indian companies would be able to offer them the salaries and facilities that are enjoying now in the US or the European countries.

On quality teachers

Another issue, which is posing as a challenge in breeding world-class talent, is quality teachers. Though there is no dearth of quality teachers in our country, I have personal experience that many of them are not paid as per the UGC guidelines. This is very unfortunate. Until and unless the teachers are paid as per the specifications and guidelines, how do you expect them to breed world-class talents. They should be paid as per their qualifications and experience and obviously the UGC pay scales should be adhered to.

Opinion**Upgradation of labs, syllabus essential**

The pharmaceutical industry is a knowledge-based industry. The industry in India is now in gearing up for the dawn of 2005 and more and more R&D strong companies are looking at drug discovery and development with the scientific talents outside India flowing back to India. This, however, makes us look back at the pharmacy educational institutions who could be the breeding centres of world-class talent. Today, the entire institutional working needs collaborative model with common broad agenda for research. There is a need for different groups like pharmaceutical chemistry, pharmacognosy, pharmacology and pharmaceuticals work with a common focus. In fact, this need can be fuelled by bodies like the AICTE, UGC, ICMR, CSIR & other funding agencies who can do a lot in this area, while funding R&D projects. There is also a need to provide basic level of education in colleges at the undergraduate level and specialised training at the post-graduate level. We need trained pharmacists to take on the supervisory roles in routine pharmaceutical manufacturing as well as pharmacists with advanced training for R&D functions. The curricula should be upgraded from time to time. Express Pharma Pulse spoke to few experts in the field:

'Research has to be focussed'

Prof B G Nagavi, Principal, JSS College of Pharmacy, Mysore, Karnataka

The need of the hour is to have intra and inter-institutional dialogue and discussion on such topics like public-private partnership, neglected diseases, policy agenda, etc. Can we afford to carry out research at high cost to address needs of developed countries? No, we can't. We need to find solutions for our problems on our own. Partnership and collaboration are the keys. Research, today, in institutions and in the country as a whole is not focused. Experts work in their own chosen areas without realising whether it is need-based for the local community or country as a whole, opine some experts.

Pharmaceutical educational institutions, especially involved in post-graduate and doctoral research programmes need to have serious discussions in the area of neglected diseases. Results can be expected after few years of concrete and sustained work.

'Industry is not the place where students can be trained from scratch'

Dr Suresh Venkataram, vice-president (Research and Development), Zydus Cadila Healthcare Ltd, Bangalore

For most part yes, but, there are some lacunae in this. While some colleges have been successful in their efforts, others have not progressed much. We are particularly lacking good training in the area of pharmaceutical analysis, which concerns me. If we have to get in to NCE discovery, a significant portion of research would be spent on drug metabolism and pharmacokinetics which rely heavily on good analytical skills as well. Industry is not the place where the students can be trained from scratch. We expect them to come in with a certain amount of knowledge. Some traditional ways of teaching has to be scrapped and new syllabus which has an inter disciplinary focus has to be added. I feel that though some colleges have resources, they do not spend much on upgrading their laboratories. They do not give adequate exposure that a student needs today.

'The curriculum should be modified to make it more industry oriented'

Dr S Gayathri Devi, Prof & Head, Dept of Pharmaceutical Marketing and Management, Al Ameen College of Pharmacy, Bangalore

There are a few MNCs in India who are strong in R&D. There are many Indians who have settled abroad and are working in pharmaceutical companies. India is left behind in terms of annual turnover as compared to the other countries in the world, since although we are more populated than most of the other countries, our moving annual total in terms of pharmaceutical formulations is less than that of Europe. Many of our bulk drug companies are engaged in export. Our formulations are also popular in African and Latin American countries.

If India has to show its presence in the pharmaceutical industry, it should work hard in the direction of preventing brain drain. At present, the lure of the dollar, the pound, shilling and riyals is causing a deep dent in

our own industry. If we can retain this talent in our country, we can show our presence in the world.

IT is one area where our Indian professionals have earned recognition the world over. They have been earning a-more-than-decent sum here in India which has contributed to the growth of the IT industry in India. If pharmaceutical industry also follows suit, we can prove to the world that India has all round talent. We should express our treasure of talent available in our country and the call of homeland that lurks our Indians can also be taken care of while still contributing to the growth of our pharmaceutical industry.

The resource of this talent lies only in pharmacy colleges who can cater to this demand of the industry. Since we require world-class talent, accreditation of institutions becomes a must. Apart from accreditation, institutes can set their own benchmarks in order to raise standards and to churn out world-class pharmacists, which eventually shall contribute to the health of the globe at large. It becomes imperative to adopt a common pharmacy syllabus for the entire country that shall be of international standard. Like in the industry, there should be an attempt made towards continuous improvement without resting on past laurels.

The curriculum can be modified to make it more industry oriented and a choice can be given for orientation towards community pharmacy. Emphasis should be laid on updating equipment in the laboratory and retrieval of information. In order to meet the needs of the industry, even personality development should be aimed at since only knowledge without the right attitude proves to be disastrous. It is at the college level itself that this grooming has to be implemented.