

## **New drug discovery - need for introspection!**

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Trend of annual NCE approvals have been alarmingly coming down from average of about 50 prior to the nineties to almost an average of below 30 in the recent times. Time appears to be right for introspection on current drug discovery research models and related tangible and intangible contributors to this trend.

Over the years, the drug discovery costs have been scaling peaks never seen before. Some of the drugs which are in the market, which are expiring or have expired, have come up with serious side effects of late. This trend has cautioned the US FDA to insist on raising the bars (safety levels) which in turn has made the new drug applications having to pass more stringent tests, leading to higher clinical expenses. Consequently, while R&D expenditures are rising, the approval rate of new drug applications are going down over the years. The NCE approvals have been coming down even though there is some encouraging trend in NME (Biologicals) (in the 2009 there have been exceptional increase in approval of Biologicals). To overcome the serious problem of rising costs of R&D (among others), there have, of late, been spate of major global level mergers and acquisitions. However, the trends of drug discovery outcomes have, in the meantime, been moving to small/medium pharma enterprises. There have been more NDAs to small/medium pharma enterprises, in recent years. The large MNCs have been in-licensing these molecules from SMEs to prevent new drug pipelines from going dry. This leads us to appreciate the statement of Prof Charles Handy that innovations come from 'fleas' and not from the "elephants". Elephants are rigid and slow in mobility and flexibility. Fleas are agile and free to move around faster. The giant pharma MNCs who are becoming 'Goliaths' by M&A route, are less likely in future to come up with breakthrough innovations, as free thinking and basic research are not encouraged any more by Corporate 'counting the money' manager. This validates the thought that new drug discovery research needs more 'Out of the Box' thinking opportunity and freedom, which appears to have been restricted by new IP/Patent regime, especially in the light of the post-Uruguay Round, post WTO/TRIPs scenario. Fewer new drugs approved, despite higher costs, no blockbuster drugs born post-WTO/TRIPs-trend leads to a need for introspection. Whether there is a need for review of the current patent-reward based drug discovery research model, is itself a matter for a brain-storming. However, it is evident that the 'Passion' which is the 'Potion' which used to drive drug discovery research, is replaced by demand for 'Patents' in fast track.

Admittedly, there have been great breakthrough drug discoveries in the past. We are enjoying the fruits thereof, through longevity, quality of life, prophylaxis and cure in new frontiers of disease. However, of late, the phenomenal new drug discoveries are rare and do not reach the target segment and the market. What is ailing the new drug discovery research? What is failing the innovative minds of the pharma research community? Among others, a visible contributory element appears to be current over emphasis on the

“patent reward” system and the corporate pressures and pulls associated with it. On analyzing the trend of new drugs which used to receive regulatory approvals in the past, they used to peak at around above 50 annually, during sixties to nineties. However, the trend started downwards from the 1990, the average falling below 30 annually. Is there any distinctively and decisively impacting research environmental factors which could have triggered this trend? Is there any factor which may have adversely impacted the innovative spirit and freedom of ‘out of the box’ thinking of the discovery community (if there is one surviving!) which I am sure like a ‘genie’ is lurking somewhere to be let out of the magic lamp.

The current thrust of the new regime of global Intellectual Properties and the ‘great gold rush’ for patent protection commenced in the early eighties manifesting itself in the Uruguay Round and the birth of WTO and TRIPs. Around the same time, a set of judicial pronouncements and ‘Doctrines’ took birth. The now famous case laws of *Diamond v. Chakrabarty*, *Integra v. Merck*, *KSR v. Teleflex*, *Festo v. Shoketsu Kinzoku Kogyo Kabushiki Co.* and Doctrines such as ‘Doctrine of Equivalents’, ‘Prosecution History Estoppel’, Doctrine of Inequitable conduct, ‘Doctrine of Double Patenting’ and ‘came to dominate patent prosecution and enforcement. The *Kodak vs. Polaroid* infringement, litigation and consequent quantum of damages awarded appears to have unduly distracted the research committees attention to patent protection rather than open innovation.

It appears that these set of events triggered the dominance of IP/Patent lawyers and their corporate manager over the drug discovery research community. The peace and tranquility, which is vital to free and innovative thinking and exploration, without urgencies and pressures of time-limits, deadlines and quick and early (often premature) disclosure for patent priority recordation appears to have a captivity and corrupting influence on the discovery community, through unrelated to drug discovery, but best described in the golden words of Tagore,

“Where the mind is without fear and the head is held high  
Where knowledge is free...” appears to me to be the missing link in the current discovery  
research atmosphere.

While cost of new drug discovery research is being met by PPP and by M&A, the results are continuing to be dismal. The new global patent regime, dictated by compulsions of TRIPs, where all type of innovations from innovation quotient of 1 to 100 receives the same period and power of protection of 20 years with associated claims of damages for infringement, appears to be influencing the corporate ‘masters’ and their ‘research fellows’ to go increasingly to pluck the low-hanging fruits. This trend has further been aggravated by the introduction of ‘drug discovery softwares’. The birth of the ‘bio-informatics’ ‘in silico’ models appears to have forced the drug discovery research community to move from ‘out of the box’ to ‘inside the box’ thinking and exploration. This trend may have shifted the emphasis from ‘disruptively innovative technologies’ and ‘serendipitous inventions’ to incremental innovations, me-too drugs and problem-solution approach which leads to early commercialization opportunities.

In older generations, the trend was to plant trees which will feed the coming generations. There was not so much greed to reap all the ‘harvests’ for oneself. Drug discovery

research would have been a 'chain' effort, without pressures of protection at early stages. Further, in the past, the progression of discovery research would have been resulting from patient, pressure-free, 'free to dream' stretch the scientific imagination and travel to new frontiers of exploratory onslaughts without worrying about the pressures of time, costs and accountability to capture the IP for protection and monetary rewards thereof. The drug discovery scientists were driven by passion and excitement to share their findings with their fraternity, leading to brainstorming and free sharing of ideas to take the 'thought' forward. Today, under pressures of confidentiality and early protection, such a 'sharing' trends have dried out. Drug discovery research cannot come from the 'Box' or from the 'Internet' or 'software'. Breakthrough innovations may need a drastic review of current discovery-research environment. In the current 'monetary reward' based research, environs may need to be pushed back into the passionate pursuit for free and truly 'out of the box' thinking and idea generation without undue pressures and corporate imprisonment of research, scientists. May be a few 'well-intentioned' 'like-minded' leaders in research science, economics and politics may need to (once again) come together to chalk out a 'free to think and act' discovery regime. May be the leading global communities should persuade the free thinking nations to come together to 'outwit the bugs', the micro-organisms and diseases-causing living organisms who have no 'patent' pressures, who keep researching and snooping on the relatively 'slow', 'incremental' discovery and innovation, research outcomes to 'outwit' the current pack of discovery scientists. Let us let the learned, well-equipped, intellectuals in the 'scientific community' to go on a hunting expedition, without worrying when and what they bring back with them. We could hope to restore and recover the glory of yesteryears by re-adopting the model which have proven to deliver in the past.