US-INDIA PARTNERSHIP IN DRUG DISCOVERY AND IN GENERICS

Report of the
Interactive workshop organized by
Asia Society and Observer Research Foundation

by

FALGUNI SEN

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on
November 20, 2007, New York

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Panelists and Participants

SEE APPENDIX 1

STRUCTURE OF THE WORKSHOP

The interactive *workshop for* invited participants began at 9 AM and Continued till 5:00 PM on Tuesday, November 20th 2007. Two panels formed the basis of the workshop. Panelists made formal presentations and/or comments. This was followed by nearly an hour-long discussion (see agenda). All presentations and discussions were taped under confidentiality.

This report is based on the transcripts of the recording as well as the formal presentations and background material.

PURPOSE OF THE REPORT

This report aims to provide policy makers and stakeholders with a roadmap to issues affecting the growth of US-India partnerships in two areas of the pharmaceutical industry: in drug discovery and in generics. It is meant to provide perspective, so that any future legislative, voluntary or other policy decision strikes an appropriate balance between two critical needs: the need for an increase in the number of relevant innovations, improving current therapeutic regimes and delivering new therapies, and the need to ethically reduce the cost of the innovative process and increase access and affordability of these therapies. Improving the effectiveness and efficiency of US-India partnerships in drug discovery and in generics will help in balancing these needs.

This report is based on an interactive stakeholder workshop hosted in November 2007 in New York as a joint enterprise of the Asia Society and the Observer Research Foundation (ORF). Forty-three participants representing a wide cross-section of stakeholders including researchers, manufacturers, Clinical Research Organizations, intellectual property experts, social entrepreneurs, NGOs, hospitals, IRBs and academicians attended the workshop (see Appendix 1).

The objective of the workshop was to discuss and debate the barriers and facilitators to the growth of US-India partnerships in drug discovery and in generics. Existing provisions and practices, gaps and the policy guidelines that need to be developed and actions to be taken by the different stakeholders in the pharmaceutical industry were discussed. A summary of the main issues from each panel is being included here. This will highlight concerns across the spectrum of stakeholders and will provide policy makers and other stakeholders with a roadmap of issues to consider in fashioning the forward path.

The emphasis in the interactive workshop was to learn from the experience of firms that had attempted to build US-India partnerships for drug discovery. The discussion was focused on capability and expertise initiatives, and barriers and facilitators to partnering in different stages of the discovery process. The panel covered target identification

and validation, lead identification and optimization, pre-clinical testing and the clinical phase. Finally, an evaluation of different models of partnership was conducted.

The emphasis in the generics panel was on identifying the issues related to Indian firms supplying generics in the US market. Discussions involved issues of quality, regulatory oversight, approvals, new business models and the role of intellectual property.

What follows is a summary of these discussions.

EXECUTIVE SUMMARY

The healthcare industry is undergoing a transformation through increased globalization, competition, cost consciousness, regulations and new technologies. In the US, spending on healthcare is expected to rise to 20% of GDP by 2015. Yet 1 in 4 workers is likely to be uninsured. There is a perception of an emerging crisis in the industry with cost and equal access to quality care as major issues.

Affordability of quality healthcare remains a concern for the majority of the population in a fast developing India as well. With the public sector contributing only 20% of all healthcare costs, individuals may spend as much as 60% of their disposable incomes on health related issues[1]. A growing middle class demand for better quality healthcare services and high disposable incomes has opened a new window of opportunities for state of the art facilities and services. With greater affluence there has been rise in diseases in the developed world such as diabetes, cardiovascular, neurological and mental health providing paradoxically, a new pool of clinical trial subjects with proper administration of ethical procedures. There is a need to learn more from practices in the US and other developed countries.

A mutual dependency has been created between India and the United States in healthcare. India has become far more integrated with the global healthcare industry especially as a preferred high quality and low cost supplier of pharmaceuticals, diagnostics, informatics, data management and elective surgeries. Within pharmaceuticals, India's importance as a supplier of new molecules, generics and pharmaceutical ingredients has increased. India has become a preferred site for efficient and speedy conduct of clinical trials. This has the potential to lower costs for healthcare In the US while it helps India develop its skills and capabilities to world-class standards.

Globally, the pharmaceutical industry is undergoing tremendous change. Downward pricing pressure, combined with an increase in cost of new drug development, has resulted in new business models. The industry is fast "de-verticalizing" with a growth in outsourcing different parts of the

1. Other private spending is by charitable trusts, insurance funds etc.

industry value chain. While India has for sometime been a major supplier of generics worldwide and has grown in contract manufacturing as well, it is becoming a preferred destination for drug discovery. Functional capabilities in chemistry, and growing abilities in biology, genetics and in bio-informatics coupled with low cost clinical trial capacity, are making India an attractive partner for drug discovery. This has been especially true after January 2005 when India became WTO/TRIPS compliant in terms of intellectual property. While "faster and cheaper" is the value proposition offered by Indian firms in the drug discovery process, it is also likely to become the source of discovery of new molecules. The likelihood of this scenario will depend on how Indian firms develop new skills and capabilities and learn the complex processes of successfully launching a new drug into the market. Much of these capabilities are being acquired through partnerships with firms in the US.

Representatives of a number of firms who have had partnerships with Indian and US firms participated in a discussion. The main issues are identified below:

1. The context is ripe for fruitful partnerships in the short term because of cost and speed, and in the long-term because of original discoveries made by Indian companies and the advantage of having a beachhead in the fast growing and ever more lucrative Indian drug market.

2. Skills in Indian firms are in alignment with the strategic objectives of the US firms. Increase in the incidence of lifestyle diseases in India fits into the needs of the developed markets. The motivation of the organizations in India to succeed gives confidence to the success of the partnerships.

3. The US firms can provide Indian firms with talent, equipment, international experience, and a culture favourable to the conduct of research in pharmaceuticals. In the short run, talent in the form of capabilities in biology, pharmacology, animal facilities, medicinal chemistry, clinical pharmacology and capacityintermsof sophisticated laboratory and diagnostics helps in getting a base set up. The possibility of being part of an integrated global site also has a lot of

learning advantages.

4. India has to build expertise and capacity to move into drug discovery effectively. In particular, appropriate capacity building needs to take place in the regulatory regime, infrastructure, training and technology. The culture of the firm needs to orient itself towards efficient discovery by encouraging innovation, a desire for intellectual property and a prime emphasis on safety. There is a lot of uncertainty in this strategy and the leadership needs to be able to offer proper guidance and vision. It also needs to motivate local talent to learn and absorb the expertise and capabilities being brought in by the US partners.

   i. In the *regulatory* realm India needs to stream line its immigration laws in order to facilitate the acquisition of global talent. In particular the process needs to be speeded up. There is a shortage of laboratory animals and laws governing their import need to be relaxed. Informed consent rules need to be properly administered and ethics committees need to develop better operating procedures to ensure GCP compliance. Greater transparency in the drug approval process and better enforcement of guidelines is needed. A patient bill of rights will also help the process.

   ii. In the *infrastructure* area more capable Phase I facilities are needed as are animal testing facilities. Ability to conduct toxicology analysis needs to be enhanced. India needs to have a more accessible healthcare system if clinical trials are to grow and informed consent to be meaningful.

   iii. There is a need for training in clinical research. There is a shortage of trained principal investigators and the few who are there are in high demand and often managing too many subjects. A number of functional areas need to improve in quality and the number of training sites needs to increase. This is particularly true of chemistry, biology, molecular biology, pharmacology, toxicology and medicinal chemistry.

   iv. Indian firms need to develop the *technological capabilities* to select

biological platforms and make more efficient use of bio-informatics. Eventually they must learn to work with less validated targets and develop their own "proof of concept" trials. They must also learn to move from targets into working with platforms in order to reap the maximum benefits from the discovery process.

v. A number of *cultural* changes need to be made within the Indian firms if they are to succeed in the drug discovery process. A culture of discovery must be cultivated. This includes becoming less risk averse.

vi. Good *leadership* is critical to the success of the drug discovery enterprise in India. Leaders have to provide the right vision and establish a culture and process where learning from the partners will indeed take place. An enthusiastic leader with a good vision can be successful in attracting highly specialized expatriate talent into the firm.

vii. The organization *must* move towards becoming an integrated drug discovery unit with proper documentation processes and functional and/or therapeutic expertise.

5. A number of different partnership models seem to be developing in India. Studies need to be done to identify whether a preferred model exists. Such partnerships may involve just fee for service contracts, build-operate-transfer (BOT) agreements, licensing agreements with royalty and milestone payments, marketing agreements or even broad- based strategic partnering without intellectual property issues clearly articulated. Indian firms have been known to engage in single client partnering as well as multi-client partnering. There are some firms that prefer to partner on specific well articulated projects while others seek a portfolio approach even with the same client. There are firms which partner with a mix of different levels of risk sometimes in as many as four therapeutic areas and five target classes. Others may take a portfolio approach but only in one therapeutic area and with the same partner. Partnerships with well aligned and long standing relationships where the Indian firm is viewed as a strategic partner and

not just a vendor seem to have longer term sustainability and the ability to move into areas of discovery that have a higher level of risk and higher potential for returns.

The main impact of generics is to be able to get good quality affordable drugs at affordable prices. This occurs in two ways: a) the price of generics is itself low and b) it forces a lowering of prices all around in the industry.

Partnerships in generics have traditionally been one of finding distribution, sales and marketing partners in US markets. To some extent there have traditionally been partnerships as contract manufacturers for a number of products including branded generics. The difference today is that some of the US firms providing such partnerships may be of Indian origin. This is because most generics manufacturers like to have a large portfolio of products and produce at a large scale. This gives them economies of scale and scope.

Generics do more than just demonstrate bioequivalence with a drug that has gone off patent (or likely to go off patent). There may be a lot of innovation that goes into the production of generics. Process innovations in terms of manufacturing efficiency, distributional and logistical efficiencies and economies of scale bring down cost. But generics companies are engaged in product innovations that lower dosages, provide "combinations" and are introducing a number of innovations in delivery systems as well. A redefined notion of a "generic" might be necessary. Such a definition will go beyond "equivalence" into defining a "generic" as anything that is low priced and necessary. Innovation without a premium price is what the new generics model is offering.

The line dividing generics companies from drug discovery companies is getting blurred. Generics firms have to learn how to compete and cooperate at the same time. Firms in India and the US have to learn how to generate trust.

There is a perception of a lack of uniform quality being produced by generics manufacturers. This is particularly true of small and medium sized firms who are trying to enter the US market. Preparing for inspections is

indeed one way to create a culture of quality. The regulatory system in India and in the US needs more capacity to do this. There are a number of opportunities for partnership between the regulatory bodies to try and increase the effectiveness of inspections and audits. Training of Indian inspectors in the US is necessary. Mere adoption of standard operating procedures (SOP) of the US is not sufficient.

It is in the best interest of Indian industry that its reputation for high quality standards in all aspects of the pharmaceutical value chain be maintained. There is a need to ensure that the "perception" of high quality is also maintained and disseminated.

Bio-generics are referred to as biosimilars in Europe and as follow-on proteins or follow-on biologics in the United States. The benefits are similar to generics. There is a need to streamline the regulatory approval process for biosimilars in India. The United States has still not provided guidances for the production and sales of follow-on biologics and a speedy decision will improve access and affordability of these drugs in the US market. India has the capability to offer the same efficiencies in biosimilars as it has for chemical entities.

Issues of intellectual property are central to the discussion on partnership in drug discovery and generics. There is a need for more debate on an optimal policy approach to the IPR regime. What does each country wish to achieve with its intellectual property laws? The answers should be based on data and research and not on special interest groups. Specifically the impact on innovation and public health of tightening up the existing Intellectual Property regime needs to be analyzed. The overall feeling was that there was a need for greater transparency worldwide in the way patents were administered so that the needed research data could be made available. Access to patent rejection and patent withdrawal data will be helpful. New patent regimes to incentivize innovations in neglected areas were also discussed. A number of alternative intellectual property initiatives are being discussed worldwide and there is a need to monitor and learn from them.

In conclusion, it is time to forge US-India partnerships in drug discovery and generics which is beneficial for both countries. India still

needs to make more changes to streamline its regulatory system and invest in training and capacity building in the areas identified above. While no single paradigm for a successful partnering model exists, building trust among the partners seems to be a necessary ingredient. US firms have to also learn more about the capabilities of Indian firms and not see their success in generics as a necessary conflict of interest. As discussed earlier, strategic objectives of the partners need alignment and where uncertainty exists, building relationships even through "fee for service" contracts helps. The entry of generics firms into the innovations space has also created opportunities for new kinds of partnership models including partnering with universities, NGOs and with one's competitors. This, in turn, poses new challenges in building trust.

BACKGROUND SITUATION

During the1990s, India's healthcare sector grew at a compound annual rate of 16%. It is around $34 billion today corresponding to approximately 6% of GDP and by some estimates likely to grow to $40 billion by 2012. In the US, spending on healthcare has risen to 1.9 trillion dollars or around 16% of GDP. Over 20% of healthcare costs in India can be directly attributed to the cost of drugs whereas in the US the percentage is around 10%. The pharmaceutical industry in the US had a market size of nearly 174 billion dollars whereas in India the size was around 7 billion dollars and is expected to grow to 20 billion dollars by 2015[2]. The drug costs, as a percentage of total healthcare costs, are likely to go up as well.

Beyond the cost of drugs is the issue of the declining number of new drugs to increase the effectiveness of existing therapies and create new therapies. This is partly being attributed to the soaring costs of new drug development. A recent study by the industry estimated the cost of development of a new biologic to be around 1.2 billion dollars[3]. The cost of drug discovery affects the overall price of drugs and the desire by pharmaceutical companies to quickly recover their investments. Increasing the number of effective drugs at a lower cost will increase the availability and affordability of new therapies. Partnerships between US and India in drug discovery will help in achieving this.

This partnership should be seen within the context of a fast changing global pharmaceutical industry. The US is responsible for nearly half the global sales of medicinal drugs and most of its profitability.

The unpopularity of formularies in managed care and public backlash against what is perceived to be runaway drug prices has reduced traditional profit margins. Governmental price controls in some countries and the success of generics have further jeopardized the financial attractiveness of many pharmaceutical companies. Higher competitive intensity in the industry has led to a reduction in exclusivity periods within popular therapeutic categories thereby reducing the premium prices that

2 McKinsey and Co. (2007), Indian Pharma 2015: Unlocking the Potential of the Indian Pharmaceuticals Market
3 PhRMA, Profile 2007

can be charged.

The pharmaceutical industry has also faced a major increase in its traditional cost structure. The estimated cost of introducing a successful drug into the market has risen from $250 million in the early 90s to around $1.2 billion for biologics in 2006. Over 60%[4] of this cost lies in clinical trials. With fewer new drugs being introduced, the cost of sales and marketing has gone up. New manufacturing regulations have increased the cost of investment in plant and equipment. The cost of litigation related to claims of adverse effects has also skyrocketed in the US, although precise estimates are not available.

There is a growing uncertainty in the pharmaceutical industry. It is unclear how genomics, proteomics, and advances in robotics and informatics will affect the processes for developing traditional therapies. The industry has responded to this uncertainty by either betting a company's financial health on one likely scenario or hedging its bets by investing in a presence in all possible scenarios. The first response is highly risky and the second one highly costly.

The industry has reacted to the margin pressures and uncertainties discussed above in a number of ways. Some are moving away from the vertically integrated "blockbuster" business model into outsourcing of a number of business processes including drug discovery, clinical trials, manufacturing, market analytics, sales education and sales force. Such companies are competing for effective marketing strategies and brand identity. Market niches are being identified and drugs developed, combined or extended to cover those niches. This has led to the growth of "enhancement" or "lifestyle" drugs. Such drugs are sold through aggressive marketing techniques usually associated with consumer products including concepts such as "lifecycle management". Industry specialists refer to this as the "deverticalization" of the pharmaceutical industry.

The industry has also taken an aggressive stance on factors exerting pressure on its profitability. Patent infringements are being more

4 Industry estimate based on interview

aggressively pursued. Patent extensions are being sought as defensive measures. Product extensions (the use of existing drugs for new therapies/indications) are being promoted. Any attempt at direct or indirect price controls is being strongly fought. Finally, the industry has also begun to consolidate and increase its efficiency and market power through mega-mergers and acquisitions.

The factors discussed above are only some of the challenges affecting the economic and global transformation of the pharmaceutical industry. That the industry has produced drugs that are effective in treating and preventing disease is no longer viewed as sufficient. What the public now looks forward is to live a longer and healthier life without costing so much. More citizen argue that health care should be a fundamental right. In this era of rapid economic and social change, reduction of cost of drug discovery and efficient use of generics can be mutually beneficial to the industry and the public.

India has recognized this opportunity to integrate its pharmaceutical industry into the global supply chain from science to discovery to manufacturing and marketing. In this "de-verticalized" industry there are a number of opportunities for Indian capabilities to address specialized needs at a lower cost and faster completion. India has also realized the potential for clinical trials and has moved forward to make the industry more conducive to partnerships. India is being presented by a number of companies as the place of choice for the conduct of clinical trials. Typically the following reasons are provided[5]:

1. **Patient base:**
   It is a country of over 1 billion people, a lot of whom need treatment for various ailments. While infectious diseases still dominate the ailing population there is an increasing percentage of people with different types of illnesses that are of concern to developed nations such as cancer, diabetes, cardio-vascular, epilepsy, alzheimer's and other lifestyle diseases[6].

5 Sen, Falguni, "Conducting Clinical Trials is there an India advantage?", The Monitor, vol. 19 (5) December 2005
6 One website (www.igatecorp.com/icri/html/aboutus/tia.htm) has the following patient population

2. **Patient type:**
Patients are multi-racial and multi-ethnic and thus provide a huge genetic variety that is going to be critical for testing the next generation of new products.

3. **Patient history:**
Patients are often "treatment naïve", thus allowing for efficacy tests not possible elsewhere.

4. **Patient recruitment:**
Subject recruitment is relatively easy and quick due to a high level of trust in the doctors and a trial being at times the only way of getting treatment.

5. **Patient retention:**
Due to the dependency of many subjects on the trial for regular medical treatment and close networks with communities where patients reside, there is a higher retention rate of subjects.

6. **Western trained principal investigators:**
Most of the principal investigators who conduct these trials have been educated in the west and are familiar with the traditions of conducting trials.

7. **State of the art specialty hospitals:**
In the last few years there have been a number of top-level hospitals with all the required equipment and infrastructure to meet ICH GCP guidelines.

8. **Communications infrastructure:**
In the first place most communication is in English; this is an advantage especially for global trials where India is one of the many sites. India has a very good IT infrastructure making data communications globally easy.

9. **Cost advantage:**
Estimates vary but 30-60% cost savings in conducting Phase III

estimate: 40 million asthmatic patients, 34 million diabetic patients, 8-10 million people HIV positive, 8 million epileptic patients, 3 million cancer patients, 2 million cardiac related deaths, 1.5 million patients with Alzheimer's disease, 15% of population is hypertensive, 1% of population suffer from schizophrenia.

trials are mentioned.

10. Progressive regulatory regime:

The regulatory system is willing to listen to and consider industry's needs.

Regulatory processes have indeed been streamlined and capacity is being built with consideration being given to issues such as patient safety, informed consent and proper training of ethics committees.

Indian firms have also leveraged their low cost and high quality manufacturing skills to become one of the major generics manufacturers. Over a third of the new applications with the USFDA for generics last year came from Indian companies.

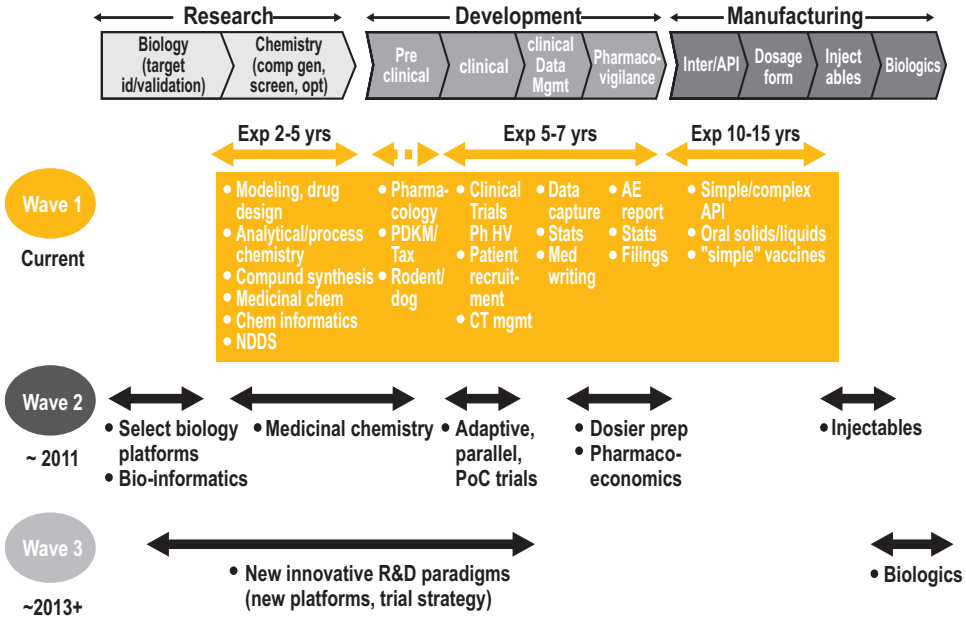
India has over 85 USFDA approved manufacturing sites the largest number in any country after the US. According to the National Pharmaceutical Policy Report of 2006, India is today recognized as one of the leading global players in the manufacture of pharmaceuticals - it holds 4th position in terms of volume and 13th in terms of value of production. It is also recognized that the cost of drugs produced in India is amongst the lowest in the world. It is estimated that by the year 2010 the pharmaceutical industry has the potential to achieve Rs 1,00,000 crores in formulations with bulk drug production going up from Rs. 8000 crores to Rs 25,000 crores.

According to a report presented by Bain and Co. to the World Economic Forum[7] in Davos, Switzerland in January 2008, Indian companies have established scale efficient manufacturing operations, with more than a decade of experience in making Active Pharmaceutical Ingredients (APIs), oral solids and liquids, and simple vaccines. This experience has, according to the report, helped create world-class Indian contract manufacturers with globally competitive cost structures. As a result, manufacturing costs in India are 30-40% less than developed markets, primarily due to lower personnel and capital construction costs. India's strength in small molecule manufacturing has resulted

7. Although occurring subsequent to the interactive workshop, this material is being referred to here due to its direct relationship to the issues discussed at the workshop in New York.

in approximately 100 FDA-approved plants, the largest number outside the US and around double that of China. India currently enjoys a 3- to 5-year head start over China in dosage form and complex API manufacturing with Indian companies also actively sourcing less costly, mass-produced simple APIs from Chin a. Indian companies are also investing significantly in drugs that are complex to manufacture such as injectables and biologics and in oncology therapeutics.

Three waves of opportunity for Pharmaceutical R&D and Manufacturing in India



Source: World Economic Forum, 24 January 2008 Davos Switzerland, prepared by Bain and Co.

SUMMARY OF ISSUES AND VIEWS

Partnering in Drug Discovery

Partnering in Generics

Conclusions

PARTNERING IN DRUG DISCOVERY

Context of partnership

Leveraging Indian capabilities/markets

Leveraging US capabilities/markets

Initiatives for expertise/capacity building

Partnership models

CONTEXT FOR PARTNERSHIPS IN DRUG DISCOVERY

A number of historical reasons have resulted in India developing capabilities in different aspects of the pharmaceutical value chain. Regulatory changes in January 2005 with WTO/TRIPS compliance have resulted in the industry re-evaluating its strategies. There is a greater impetus to integrate itself into the global supply chain. A number of firms have done this through becoming suppliers to and partnering with global pharmaceutical firms.

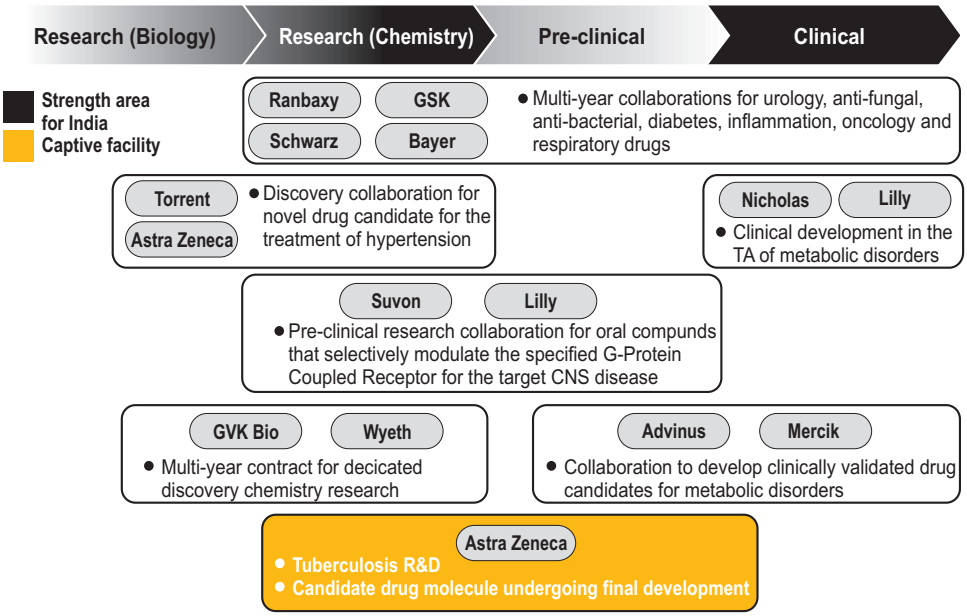
Outsourcing to Indian firms has happened for some time now. Indian firms started with functional outsourcing in areas such as process chemistry and the manufacture of intermediates. They moved to value added areas and began an emphasis on doing more biology. Pre-clinical development in the private sector (mostly rodents) was then established to match some of the work being done in governmental laboratories and universities. Soon thereafter some firms began to get IP critical projects while the API and formulation businesses began to grow. This was followed by a growth in the synthesis business and lead optimization. Work on functional biology was started by the industry with toxicity and medicinal chemistry capabilities being developed. In the last two years or so licensing at pre-clinical stage and Phase I has occurred and we are beginning to see partnerships with developmental rights.

Although drug discovery in India is a relatively new phenomenon and thus far very few compounds have really been discovered in India, the potential for success is high. Cost and speed have been the primary value proposition provided by Indian firms. However, talent and specialized knowledge in new technologies may become the source of competitive advantage.

Reducing cost of drug discovery is critical to the long-term viability of global pharmaceutical industry. Building capabilities in India is vital in ensuring such a reduction in costs. It is estimated that research costs for chemical entities are around 40% of the costs in developed countries and the costs for conducting clinical trials can be anywhere between 30-60% cheaper. Trials are also completed faster allowing early entry in large markets. A three month entry advantage in a billion dollar market provides an additional $250 million revenue to the pharmaceutical company. Even universities in the US are looking for Phase I support from India in order to generate higher possible revenues from their discoveries. Thus, India firms can become highly beneficial partners to their US counter parts in drug discovery. In the future, as India builds its capabilities in new

technologies it can become a source for innovations produced much more cheaply. Given that the predicted size of the Indian drug market is likely to grow to $20 billion by 2015 and the likely size of the patented drug market (of around $2 Billion by 2015)[8], US firms may find an Indian partner as a facilitator to market entry. On the other hand, India needs these partnerships in order to build its capabilities into next generation platform technologies. The figure below identifies some such partnerships leveraging the current strengths of the Indian firms.

Partnering by Indian firms



Source: Company websites; News articles

Source: World Economic Forum, 24 January 2008 Davos Switzerland, prepared by Bain and Co

8 Estimated at 10% of the total market

Partnerships are occurring within a number of different frameworks. There is the traditional outsourcing model, strategic alliances (with and without venture financing) and joint ventures. The large number of start-ups in the US, especially in the biotechnology space, makes them conducive to partnerships in the strategic alliance mode.

Indian industry feels that there needs to be more support for R&D from the government. They claim that only 10% of what they spend on R&D comes through fiscal incentives. While in the US there was an opinion that over 50% of what industry spends on R&D comes through matching grants. Indian industry spent almost $520 million in R&D in 2006, which is a significant improvement from $30 million in 1995. Thus the growth rate in R&D spending is phenomenal although the actual numbers may not be that high (compared to over $40 billion by multinationals in the US). Indian firms can demonstrate a breakthrough in costs of R&D by bringing it down from $1.2 billion to around 200 million. That is a one-sixth reduction in costs. There are already 39-40 molecules that were developed in India that have INDs approval and four of them are entering Phase III. Thus we may soon see a fully Indian developed molecule introduced into the market by 2010-2011.

LEVERAGING INDIAN CAPABILITIES AND MARKETS

US firms have indeed shown a growing interest in partnering with Indian firms in drug discovery. Besides cost and speed they see the growing interest and relevance of lifestyle diseases in India. The best talent pool in India is more attracted to work in areas such as oncology, cardio-vascular diseases, CNS, diabetes and other such lifestyle categories as opposed to anti-infectives. There is also interest in vaccines. These fit into the objectives of the US firms. Not only is the scientific talent aligned with the interests of the developed markets but the increase in the incidence of these diseases in India also allows for speedy recruiting of subjects and execution of trials in these areas.

Unburdened by huge costs of liability suits, there is a greater culture of risk taking or at least a "lack of overkill on unnecessary safety issues" that the US partners find attractive. While this may cause concern regarding patient and workplace safety issues there is a "shackled" feeling in the industry by unnecessary legislation and bureaucratic steps required to avoid liability. The fewer steps in Indian firms are thus attractive to the US partners.

Indian firms are "hungry" for results. There is a high degree of motivation due to the possible benefits and the sheer energy of working on the cutting edges of the field an opportunity accorded by the partnerships many Indian firms have leaders who have taken personal responsibility for steering their firm in the direction of partnerships in order to acquire capabilities that will bear fruit 5-10 years later. There is a desire to show success and demonstrate positive results within a reasonable period. This positive and energetic attitude is welcomed by the US counterparts.

Finally, a US firm may not wish to invest in a large-scale operation in India. Allowing an Indian partner to build their capacity with a number of other firms enables them to generate scale efficiencies without high levels of investment. As and when the Indian market develops, the US firm now finds itself in a position to leverage their Indian partner to access that market.

While cost and speed remain two of the main drivers of partnerships with Indian firms in drug discovery, the availability of talent due to a number of post-docs returning to India with required skills is an added attraction. Traditional medicine is developing in a more sophisticated way in India now and is becoming a viable source of knowledge for new molecules. The diversity of plant products in India, genetic diversity of its population and movement in the stem-cell research with fewer restrictions are other motivators for partnerships. Finally innovative financing available in India can also foster partnerships especially with start-ups in the US, which lack the cash-flow to optimize leads and conduct clinical trials. Some Indian firms have created alliances with global biotech funds thus allowing them to develop innovative financing and create alliances.

Partnerships are occurring at all stages of the drug discovery process. Beyond pre-clinical and clinical trials there is evidence of such partnerships in specific services such as high throughput screening, miniaturized experiments, setting up biological screening systems and informatics; stem cell and tissue engineering; animal models; *in vivo* imaging; molecular medicine, genetic characterization, diagnostic based differentiation ; medical writing, data management, bio-statistics, integrating pharm acovigilance databases, databases, centralized imaging and ECG reading services among others.

LEVERAGING US CAPABILITIES AND MARKETS

Indian firms do not have adequate expertise in drug discovery. The US firms can provide them with talent, equipment, international experience, and a culture favourable to the conduct of research in pharmaceuticals.

In the short run, talent in the form of capabilities in biology, pharmacology, animal facilities, medicinal chemistry, clinical pharmacology and capacity in terms of sophisticated laboratory and diagnostics helps in getting a base set up. The possibility of being part of an integrated global site also has a lot of learning advantages.

It is however, crucial that the objectives of the US and Indian partners are well aligned. It is especially important that all intellectual property issues and marketing rights are properly negotiated and agreed upon from the very beginning of the relationship. Contracts sometimes may have restrictive clauses that exclude the Indian firm from using the knowledge and skills developed from one partnership for other projects of the firm. Usually these have been found to be not in the long-term interest of the Indian firm although exceptions do exist. In any event the long-term impact of such restrictions needs to be properly evaluated.

INITIATIVES FOR EXPERTISE BUILDING

India has to build expertise and capacity to move into drug discovery effectively. In particular, appropriate capacity needs to be built in the regulatory regime, infrastructure, training, and technology. The culture of the firm needs to orient itself towards efficient discovery by encouraging innovation, a desire for intellectual property and a prime emphasis on safety. There is a lot of uncertainty in this strategy and the leadership needs to be in a position to offer proper guidance and vision. It also needs to motivate local talent to learn and absorb the expertise and capabilities being brought in by the US partners.

Regulatory regime:

Already much has been done in India to improve the regulatory regime. The newly formed National Drug Authority will indeed coordinate the needs of different departments and ministries and will harmonize them with those of the US. Technical assistance is being sought from the USFDA to set up the NDA. Although it is expected that full operationalization of this authority may take six to seven years, it is a step in the right direction. The authority also promises more transparency and alignment with best practices in the developed world. This authority will regulate biotech and medical devices as well.

The government is also setting up a system used by FDA for quick clearances. A clinical trial registry is already operational in conformity with the suggestions of WHO. Guidelines for research and therapy are being put on the websites. Clinical trial principal investigators and teams will have to follow best practices of US and Europe. Harmonization of regulations is ensuring compliance with both the US and the European commission. In general the expectation is that there will be more transparency in each stage of the process accompanied by greater oversight and compliance. The proactive efforts being made to develop regulatory norms for therapeutic nano particles are also a step in the right direction.

GCP audits will be more frequent to ensure quality and safety. Although there is a shortage of GCP trained auditors, this situation is changing. Most clinical trial approval processes have been clarified although some confusion may still exist regarding Phase I trials for

molecules developed outside India where no concurrent trials elsewhere are being planned. By and large these too are being approved as long as some "need to the nation" can be demonstrated. It should be noted that there are 36-38 molecules in trials at the moment after Phase I was completed in India.

Informed consent is an issue in all countries where clinical trials are conducted and human subjects are used. In India, there has been some success in vaccine trials in enhancing the quality of informed consent by involving the community from which the subjects are drawn. This may be extended to all trials and the best practices should be adopted as standard operating procedures for all informed consent.

Although land has been acquired for housing large animals for testing and a primate breeding and experimental facility is being opened up, there is a shortage of animals other than rodents and dogs. Regulations governing the import of animals for trials need to be made more efficient.

The government has put aside some funds for public-private partnerships in drug discovery but these are not adequately publicized and are poorly administered. More clarity regarding government-industry participation is needed especially regarding collaboration with government- owned research institutes.

There is a shortage of talent in some key areas. Although it is possible to find such talent abroad, Indian immigration laws are very cumbersome and create inordinate delays. This adversely affects the competitive advantage of Indian firms and complicate the implementation of the partnership relationships.

There is a need to create a patient bill of rights. This will clarify the expectations and responsibilities on both sides.

Infrastructure:

India has invested in the development of a lot of infrastructure in drug discovery. While the government has done most of the investing, the private sector has also recently made some major investments. Animal testing capabilities remain a major lacuna in all areas except

rodents and, of late, dogs.

While the recent investments in enhancing the clinical research capabilities of 10 major medical schools is a positive step, certified laboratory and imaging diagnostics needed for clinical trials are grossly inadequate.

While the government has developed capacity in BSL3 and 4 level facilities their utilization by the private sector is doubtful. In general more strategic investments are needed with the collaboration of the private sector for the research and pre-clinical stages of the drug discovery process. There is a need for more quality centres for Phase I trials in private and government hospitals.

India has to develop more capabilities in toxicology. This includes both human resources and infrastructure capabilities as this is vital to the early stage development of drugs.

Availability of healthcare is an assumption that guides best practices of human subject enrollment for clinical trials. Until India can assure more adequate healthcare for all, there will always be the suspicion that the informed consent by subjects is being given only to get basic healthcare. This can sully the reputation of India as a preferred site for clinical trials.

Training:

There is a need to fill the shortage of trained principal investigators because the few who are there are in high demand and often managing too many subjects. The existing training programmes in clinical research are inadequate. The recent collaboration with NIH to offer training in India for a Masters In Clinical Research is a step towards achieving this objective.

A number of functional areas need to improve in quality, and the number of training sites. This is particularly true of chemistry, biology, molecular biology, pharmacology, toxicology and medicinal chemistry.

Technology:

Indian firms need to develop the technological capabilities to select biological platforms and make more efficient use of bio-informatics.

Eventually they must learn to work with less validated targets and develop their own "proof of concept" trials. They must also learn to move from targets into working with platforms in order to derive maximum benefits from the discovery process.

Culture:

A number of cultural changes need to fall in place within the Indian firms if they are to succeed in the drug discovery process. A culture of discovery must be nurtured. This may vary from firm to firm but includes a sense of excitement about research, a sense of discipline in every aspect of the process, an inner desire to create intellectual property and an intrinsic motivation to succeed.

Such firms should also have human resource policies, which match the expectations of their intelligent young scientists and an atmosphere that makes them feel valued and an integral part of the system.

Firms in India are often risk averse. While it may be possible to be part of the drug discovery process in a "fee for service" mode it is difficult for such firms to move on to more value added roles. To do this the firm has to recognize that there is a risk return relationship and a culture of risk taking may benefit long-term learning and capability building which will eventually yield higher returns.

Leadership:

Quality leadership is key to the success of the drug discovery enterprise in India especially when partnerships with firms abroad are involved. Such leaders have to not only provide the right vision, establish a culture and process where learning from the partners will indeed take place but will also have to create an atmosphere of "having fun". This playfulness is central to the creative process in drug discovery leadership should be able to attract the proper talent. An enthusiastic leader with a good vision can be successful in attracting highly specialized expatriate talent into the firm.

Organizational:

A partnership in drug discovery where the Indian partner has an already established integrated drug discovery unit or is likely to develop

such an integrated unit through the partnership seems to be preferred. Indian firms have a preference for US partners who come to them with integrated global sites for different stages of the drug discovery process.

One of the important element of a successful partnership in the discovery process is the foolproof ability to properly document different aspects of the process and integrate the documentation with different global sites. Such a documentation capability goes beyond operating procedures and technology and is dependent on a culture that fosters and emphasizes the importance of such documentation.

An Indian firm seeking a successful partnership will also need to decide on whether to emphasize vertical expertise in a particular therapeutic category. While this may prove to be advantageous for eventual value added developments, in the short run it may restrict the possibilities of multiple revenue streams for the Indian partner.

PARTNERSHIP MODELS

There are a number of new areas of partnership in the drug discovery segment that are of relevance to Indian firms. Partnerships are being sought with US firms, European firms, universities in the US and in India, Government institutions and departments, and financial institutions. Such partnerships may involve just fee for service contracts, build-operate-transfer (BOT) agreements, licensing agreements with royalty and milestone payments, marketing agreements or even broad-based strategic partnering without intellectual property issues clearly articulated.

Indian firms are known to engage in single client partnering as well as multi-client partnering. Some have focused on a single mode of partnership such as fee for service while others have engaged in multi-modes of partnering such as fee for service with one firm, licensing with royalty payments with another, exclusive marketing rights in some markets and joint ownership of molecule in others.

There are some firms that prefer to partner on specific well articulated projects while others seek a portfolio approach even with the same client. There are firms which partner with a mix of different levels of risk in four therapeutic areas and five target classes. Others may take a portfolio approach but only in one therapeutic area and with the same partner.

It is not clear which approach is the most effective. However, partnerships with well aligned and long standing relationships where the Indian firm is viewed as a partner and not a vendor seem to have longer term sustainability and the ability to move into areas of discovery that have a higher level of risk. Pure fee for service contracts have fewer chances of developing competitive advantage through knowledge gained from such contracts. Studies need to be done on an ongoing basis to learn from best practices of others regarding the preferred model for partnering in different contexts.

It is argned by some that partnering in vaccines is different from the rest. While trust is an important dimension of all partnering relationships this has to be effectively put into operating procedures of both the

partnering firms and the objectives very carefully aligned.This partly is because the public is more involved in scrutinizing vaccine development and there are more complexities in conducting clinical trials in this area.

While open-ended Intellectual Property arrangements based on trust can work in the very early stages of the drug discovery process, it is advisable to negotiate this issue well in advance in any partnership. Open-ended agreements may be viable in a fee for service mode where the objective of the Indian company is primarily to generate enough scale of work so that investments in in-house capabilities can be adequately made. Having multiple clients does not appear to be a problem in partnering as long as proper firewalls exist. The portfolio management approach of multiple therapeutic areas, and multiple target classes has also been known to be successful. However, for the Indian firm to have a generics manufacturing arm while it is trying to develop an integrated drug discovery unit through partnership can become a problem. This may be due to external reasons such as conflict of interest in specific markets or therapeutic categories with its clients and thus the difficulty in generating the required level of mutual trust. Or it could be an internal issue of inability to emphasize in the same organization a culture of efficiency with a culture of innovation. Thus a number of Indian firms are spinning off their drug discovery units.

Indian firms need to understand the types of targets that are being offered by US firms for partnership in discovery. Evaluation of the risks is complex and depends on the ability of the Indian firm to acquire the knowledge, skills and appropriate information regarding the targets to make these assessments. This risk assessment is critical in forging a meaningful partnership and more effort must be put into it.

Some Indian firms, which are already developed in their drug discovery capabilities, may need to assess the strategic timing for moving away from targets into platforms. Partnerships in platform development are different as the risk sharing is much higher, but then so are the possible returns. Creating partnership agreements for sharing the development of platforms needs high level of skills for assessing risks and potentials for revenue streams and thus the type of intellectual property to be shared by the partnering companies.

Some US firms have developed sophisticated milestone payment models that they use in negotiating partnership agreements. Indian firms need to build or seek this expertise before they enter into negotiations.

Another way of acquiring needed skills and assets for an Indian firm is to globalize by buying such assets in the developing countries. There is some evidence of this already where a firm's long-term strategy is well developed and core assets are being purchased rather than licensed or partnered. Similarly, US firms are developing strategies of acquiring core assets in India through equity partnerships and other means.

Finally, Indian firms are known to be reluctant to apply for funds to agencies such as WHO and others. They need to seize the opportunities still existing in the area. The government can play a more proactive role in collecting and disseminating this kind of information.

PARTNERSHIPS IN GENERICS

Context of Partnerships

Generics and innovation

Quality and Regulation

Biosimilars

Intellectual Property

CONTEXT OF PARTNERSHIPS

As recently as 1989 india was a net importer of medicines. In less than two decades half of India's production is being exported to the world and half of these exports are in turn to Europe and North America. No drug master filings (DMF) were made in the US before 1995 when the TRIPS agreement was signed. Since then the growth has been phenomenal from patent filings to over 50% of the Paragraph 4 challenges. Indian industry is looking for value added ways to gain advantage in generics and in ways to innovate.

The main impact of generics is to be able to get good quality affordable drugs at affordable prices. This occurs in two ways: a) the price of generics is itself low and b) it forces a lowering of prices all around in the industry. Lower prices increase the number of people worldwide who can afford the medication, use it in a more continuous manner and not cut dosages for the sake of affordability. This in turn lowers the overall healthcare burden. Lower prices also increase the volume of sales since there is still a large percentage of people worldwide who are required to pay for their medication and are thus price sensitive. This increase in volume may increase the total profits to the industry even though some players see a major drop in margins.

GENERICS AND INNOVATION

There are probably twenty generics companies of Indian origin operating globally. Half of API filings in the US are from firms of Indian origin and so are a third of all ANDAs. They have a presence in the entire value chain from API development to commercial scale manufacture to product formulations to manufacturing of formulations to distribution and finally to sales and marketing. Generics firms are competing on scale and high levels of vertical integration while toying with the possibilities of contracting out some parts to get better scale economies and new revenues. This is happening in parts of the value chain such as sales and marketing.

Generics do more than just demonstrate bioequivalence with a drug that has gone off patent (or likely to go off patent). There may be a lot of innovation that goes into the production of generics. Process innovations in terms of manufacturing efficiency, distributional and Logistical efficiencies and economies of scale bring down cost. But generics companies are engaged in product innovations as well. Many firms are developing capabilities in "reformulation" work and the traditional boundaries set by the Waxman-Hatch act are getting blurred. Generics firms are creating innovations that lower dosages and thus get higher compliance (with all its accompanying benefits). They are succeeding in developing "combinations" where the original innovators were a number of different companies. This is reducing the costs and creating efficiencies in therapeutic outcomes.Generics companies are introducing a number of innovations in delivery systems as well (such as patches, injectables, delayed release etc.). A redefined notion of a "generic" might be necessary. Such a definition will go beyond "equivalence" into defining a "generic" as anything that is low priced and necessary. Innovation without a premium price is what the new generics model is offering.

Generics companies were traditionally expected to compete on scale and efficiency and not on innovation. As the generics space has become highly competitive these firms have moved into the innovation space in order to create unique selling propositions for their products and maybe even generate premium pricing in a low price environment. This has

required them to acquire critical innovation skills. These skills have now enabled them to seriously think of entering the drug discovery part of the value chain as well since a lot of their innovations require going through clinical trials as well. This has ironically brought them into possibilities of partnership in the drug discovery arena. While competing with many pharmaceutical companies these generics firms would also like to cooperate with them in bringing out a number of innovations.

Much has been written about "co-opetition" and the complex structures and culture it requires to succeed. Spinning off the innovation arms of their companies is one such new structure that the Indian generics companies are moving towards. Purchasing innovation assets globally, along with generating manufacturing scale is another strategy being adopted. Generating trust is an area that US and Indian firms have to learn in order to successfully compete and cooperate.

PARTNERSHIP FOR QUALITY AND REGULATION

There is a perception that uniform quality lacks in products manufactured by generics firms. This is due to multiple products produced by the same firm using the same manufacturing technologies requiring numerous stoppages and clean ups and other manual operations susceptible to errors. While there is no evidence of this with the large generics manufacturers there is a concern as a number of small and medium sized firms from India begin to find distribution channels in the United States and other countries. Some of the large generics manufacturers are indeed providing such channels in order to get proper scale in their sales and marketing functions.

Preparing for inspections does create a culture of quality. Indian firms do not have the advantage of really detailed FDA inspections as the inspectors stay for very few days. The Indian inspectors may also not be as effective. The firms have to self regulate quality. However, an Indian company goes through numerous approval processes. The United States is the last in line. Typically a firm will first get approval to enter South Africa, then Australia, UK, Europe and finally the United States. Requirements for each of these countries are often different. The Indian firm is well advised to pick the best practice in each of the categories for approval. If they do this, their compliance with USFDA will be more than satisfactory.

There is however, good reason to increase the regulatory capacity of the DCGI in India. USFDA inspectors are in India but their capacity is highly limited. They may be encouraged to have Indian inspectors accompany them. This will make their work more efficient as well as be a training opportunity for the Indian inspectors. Indian audit reports may also be used as input to inspections by other countries. There has been a suggestion to locate a senior US inspector in India with junior level trainees. Due to political reasons the USFDA does not acknowledge the presence of inspectors/office in India. However, there is an acknowledgement that regulatory capacity is limited and yet high quality inspections are indeed helpful in maintaining quality in operations. There is need for regulatory partnership. There is already a developing collaboration between FICCI, IPA, USFDA, and the office of the DCGI for

GMP and GCP. Training of Indian inspectors in the US is necessary. Adoption of standard operating procedures (SOP) is not sufficient. The Indian industry is pushing for bringing Indian regulatory infrastructure to UDFDA level. This may require the levy of user fees, which the industry has not opposed.

It is in the best interest of Indian industry that its reputation for high quality standards in all aspects of the pharmaceutical value chain be maintained. There is a need to ensure that the "perception" of high quality is also maintained and disseminated. Regulatory partnerships are fraught with perception problems and appearances of conflicts of interest. Care must be taken in such situations to keep the perception of quality and integrity paramount.

BIOSIMILARS

Bio-generics are referred to as biosimilars in Europe and as follow-on proteins or follow-on biologics in the United States. The benefits are similar to generics although the industry estimates the drop in price will be less (20-40% as opposed to 80-90% for chemical entities).Part of the reason for this may be the very few players in the biosimilar field unable to impact the industry as much. The need for more tests such as limited phase III trials may increase the cost/price. Increased regulatory complexity to determine equivalence may also indirectly contribute to the price. However, the market is expected to grow at around 20% to an overall size of around $35 billion worldwide. This growth is likely to compensate for the drop in price due to the introduction of biosimilars. In India, around 15 biosimilar products have been introduced in the last 5 years and growing very fast with a price reduction of around 30-40%.

In Europe there are six products that have been approved for biosimilars and guidances have been issued regarding the approvals of simple proteins that are relatively easy to manufacture. In India and China biosimilars are approved on a case-to-case basis with toxicity studies and limited phase III trials. There is no special manufacturing licensing provision different from those of innovative products. A number of different agencies get involved in the approval of production of biologics in India although the creation of the National Drug Authority and other coordinating committees should streamline the process in the near future. Although India does not have the long experience of manufacturing biologics it has developed some very efficient manufacturing capabilities and scalable capacity. This should allow Indian companies to demonstrate the same kind of competitive advantage in cost and high quality that they have shown in the area of generics. Process improvements, innovations in manufacturing and quality commitment along with skilled labor are some of India's advantages. The speed of clinical trials is also a source of advantage to Indian firms. The United States has still not provided guidances for the production and sales of follow-on biologics and a speedy decision will improve access and affordability of these drugs in the US market.Clarification of some of the laws in India regarding contract manufacturing in the area of biologics will

also help Indian firms to capitalize on the intermittent capacity utilization problem that innovator firms in this area have faced. Such an experience will also prepare them better for entry into the biosimilar market.

INTELLECTUAL PROPERTY

Issues of intellectual property are central to the discussion on partnership in drug discovery and generics. Where relevant they have been included in the discussions above. There is however, a need for more debate on an optimal policy approach to the IPR regime. What does each country wish to achieve with its intellectual property laws? These laws have historical significance in all countries and some elements may be a relic of the past needing urgent change to keep up with developments in technology and globalization.

This may be more true of India which has had some major changes made to its IPR regime since signing the TRIPs agreement. The impact of this agreement is still being felt and more research and data based policy decisions may be needed as opposed to pressure from special interests. Research needs to find answers to a number of questions such as:

a. What is the impact on public health, affordability and the tightening of IPR in India?

b. Will a tighter IPR regime help in making the industry more innovative or will it force consolidation of small and medium sized pharmaceutical enterprises?

c. Will a tighter regime on minor improvements (such as combinations, dosages, delivery systems, new indications) as opposed to new molecules help or hinder the development of the pharmaceutical industry in terms of manufacturing quality and capacity, drug discovery and transfer of skills and capabilities through partnerships?

d. Does a tighter IPR regime in India matter to Indian firms or US firms in developing new partnerships? Is there a short-term versus a long-term difference in this when the Indian market grows to $20 billion by 2015 (although only $2 billion of that is expected to be the patented drugs part)?

e. What difference will clarification in the definition of "efficacy" in section3(d) make?

f. Is the IPR regime in India seen as a way of incentivizing the industry to move in a particular direction? If so, what is that direction?

g. Since the US market is 50% of the global market and has a tight IP regime and given that Indian firms really want to access that market for new discoveries and follow-on innovations, does the IPR regime in India really matter?

h. How to structure the IPR regime so that national priorities of neglected diseases and other public health issues can get priority resource allocations? And, how to achieve this within the TRIPS agreement?

These questions were raised in the workshop. The overall feeling was that there was a need for greater transparency worldwide in the way patents were administered so that the needed research data could be made available. Some other suggestions were that:

1. Patent applications title should be in the international non-proprietary name;

2. Databases of rejected patent applications be made available;

3. Databases of withdrawn applications are made available.

Beyond the patent regime the workshop discussed the need to look into the trade secrets act. There is a lot of proprietary information that is kept confidential through this act. There is a concern with a fast growing industry such as pharmaceuticals in India that skilled employees from one firm may be easily "poached" by others and that such an increase in human turnover could jeopardize confidentiality unless the law preserves trade secrets.

Dissatisfaction with the pharmaceutical industry has generated a number of alternative options of meeting the twin goals of innovation

and accessibility. Some influential members are arguing for a greater governmental role in funding innovations in pharmaceutical industry while preserving the possible returns of such innovations in the public domain. Others are discussing philanthropic options in order to guarantee that innovations for which a market may not be as lucrative are also created and implemented. Yet others are pushing for advanced market commitments as a way of providing incentives for needed innovations.

One of the options discussed at the workshop was a new initiative (www.patent2.org) to offer a second stream of patents that would reward firms based on the global impact on the disease "cured" by the innovation. This is seen as a supplement to existing patent law. Thus a successful innovation will get the most return to the sponsor if it has the largest impact on the global disease burden or is used by the largest number of people. There will be an incentive to produce and sell such innovations to as many people as possible at as low a price such that the global impact will be maximized. Operationalization of this system still needs to be done. Methods for the determination of "global impact" attributable to a single innovation is the most problematic.

CONCLUSIONS

In conclusion, US-India partnerships in drug discovery appear to be necessary for both countries and the timing is right. India still needs to make some changes to streamline its regulatory system and invest in training and capacity building in the areas identified above. While no single paradigm for a successful partnering model exists as yet building trust among the partners seems to be a necessary ingredient. US firms have to also learn more about the capabilities of Indian firms and not see their success with generics as a necessary conflict of interest. As discussed earlier, strategic objectives of the partners need alignment and where uncertainty exists, building relationships even through "fee for service" projects helps.

Partnership in generics is of a different form. Indian firms are active in all parts of the generic value chain. In some cases partnership is of a small or medium sized Indian firm with the sales and marketing unit of a larger Indian firm located in the United States. However, there is a new business model for generics, which sees them as providing not just low price but needed value. Generics firms are innovating in formulations and delivery systems to create unique selling propositions and provide necessary value at a low price. Partnerships with the original innovators in manufacturing and incremental innovations are possible as are new partners such as universities, NGOs and others.

Indian capacity in the regulatory arena needs to improve in order to maintain the perception and reality of quality in Indian manufactured generics. Much of this can happen through partnerships with US firms and other regulatory bodies. Similarly, the US regulators need to develop guidances regarding biosimilars (follow-on biologics). Indian firms can increase affordability of drugs in this arena in the US as well. They have demonstrated this capability in India and in Europe.

Intellectual property remains a major issue in creating partnerships in drug discovery and generics. And yet, its actual importance has been difficult to determine. There is a need for more research and data-based dialog on this issue. Greater transparency and availability of data in this regard will go a long way. This workshop concluded on a positive note

regarding partnerships in drug discovery and in generics between Indian and US firms in the pharmaceutical industry. There is potential for improvement in efficiency, capacity development and regulatory mechanisms. However, there was a feeling that the developments were in the right direction.

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The healthcare industry is undergoing an unprecedented change. The affordability and quality of healthcare are being profoundly affected by increased globalization, competition, cost consciousness, regulations and new technologies. The U.S. is expected to spend up to 20% of GDP on healthcare by 2015. Yet 1 in 4 workers remain uninsured. This crisis in healthcare access also extends to the majority of the population in India. With public spending contributing a mere 20% of India's total healthcare cost, up to 60% of individual income goes toward health related expenses. Growing affluence of the middle class demands better quality healthcare and creates new opportunities for state-of-the-art facilities and services.

The workshop on US-*India Partnership in Drug Discovery and in Generics Organized* by the Observer Research Foundation and the Asia Society brought together stakeholders from India and the US where issues critical to the coordination of public policy and firm-level strategies in the two countries were discussed. Participants were drawn from regulatory bodies, pharmaceutical companies, clinical research organizations, hospitals, institutional review boards, managed care companies, insurance companies, biotech companies, diagnostics companies, patient advocacy groups and bioethics experts. The conference underscored the increased potential for partnership in healthcare between the U.S. and India. India's emergence as a preferred high-quality and low-cost supplier in the global healthcare industry may help the US lower its healthcare cost, while the US may help India in developing the skills and capabilities of its workforce. Common concerns and policy recommendations for US and India, and areas for further study and future actions, were identified at the workshop.

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