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Promoting R&D in Preventive Health Technologies:

Opportunities for the Indian Pharmaceutical and Biotechnology Sector

IAVI-India

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Please refer to Annex I for a complete list of participants.

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Opportunities for the Indian Pharmaceutical and Biotechnology Sector

An IAVI-Led Workshop
New Delhi, India

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IAVI's Policy Research Working Paper series disseminates the findings of works in progress to promote the exchange of ideas about the effective development and global distribution of vaccines to prevent HIV infection.

Contents

Acronyms and Abbreviations

AIDS	Acquired Immune Deficiency Syndrome
CRO	Clinical Research Organisations
CSIR	Council of Scientific & Industrial Research (India)
EU	European Union
FDA	Food & Drug Administration (United States)
GDP	Gross Domestic Product
HIV	Human Immunodeficiency Virus
IAVI	International AIDS Vaccine Initiative
ICMR	Indian Council of Medical Research
IDC	Innovative Developing Country
IPR	Intellectual Property Rights
NACO	National AIDS Control Organisation (India)
NGO	Non-governmental organization
NIH	National Institutes of Health (United States)
NMITLI	New Millennium Indian Technology Leadership Initiative
OECD	Organisation for Economic Cooperation and Development
PPP	Public-private partnership
R&D	Research & development
TRIPS	Trade-Related Aspects of Intellectual Property Rights

Introduction

AIDS is the greatest public health crisis of our time. It is critical that global initiatives incorporate both short and long term perspectives. Over the longer term we need to support the development of better preventive tools, especially a vaccine, which has been key to ending viral epidemics.

The International AIDS Vaccine Initiative (IAVI) is a not-for-profit, public-private partnership with a mission to ensure the development of a preventive AIDS vaccine, which will be accessible to all. Since its founding, IAVI has grown into the world's largest organisation focused solely on AIDS vaccine development, now operational in 23 countries. With its partners IAVI has taken six candidate vaccines into human trials in nine countries. The need to engage the private sector in this endeavour has always been a priority for IAVI. Most product development expertise rests in the private sector companies. These companies have traditionally played the lead role in translating important basic research – which is mostly carried out by government research agencies and academic institutions – into products that can be manufactured at large scale for commercial use.

Given the increasing strength of the pharmaceutical and biotechnology sector in developing countries such as India (as well as Brazil, China, and others), IAVI is convinced that meaningful progress can be achieved in the global field of AIDS vaccine R&D. Additionally, given that AIDS is a challenge that is more immediately and urgently relevant to the developing world – as opposed to the developed world – there are compelling reasons (both commercial and social) for Indian industry to actively engage in finding solutions.

The workshop, "Promoting R&D in Preventive Health Technologies," with a specific focus on preventive AIDS vaccines, highlighted the market opportunities for Indian industry and addressed some of the challenges (scientific, market-related and policy-related) that have constrained companies from participating more aggressively. Deliberations at the workshop, which took place in New Delhi, India on December 3, 2004, focused on identifying mechanisms aimed at creating a more conducive policy regime, examined areas of potential interest for Indian industry to undertake R&D efforts in this area and explored innovative models of partnership.

This paper summarises the proceedings of the workshop, which was chaired by Kapil Sibal, Minister of State for Science & Technology. The first part of this paper encapsulates the workshop presentations and dialogues, while the second part draws together the main findings of the workshop and outlines the way forward.

I. Session 1: A Global Overview and Assessment of Current R&D Efforts in AIDS Vaccine Research

Dr Seth Berkley, CEO & President, IAVI

Dr Berkley provided an overview that focused on two broad topics: a global perspective on AIDS vaccine development efforts; and the status of vaccine development efforts in the Indian pharmaceutical sector. He also made suggestions towards incentivising R&D in India.

Background

Ten years ago, R&D efforts towards developing an AIDS vaccine were nascent. The pipeline of vaccines was very limited. There was scant investment (or interest) by either the public or the private sector and few active advocates. No vaccines had been tested, and there was no political leadership in the developing world in this regard.

What was the cause of this situation? IAVI identified three limiting factors:

- The **private sector** has the skill sets required to develop a vaccine, but only limited commercial incentives to invest heavily in vaccine R&D
- The **public sector** is best at funding pure research, but lacks product development capabilities. Moreover, it tends to be 'national' (rather than 'global') in its outlook
- The **UN and other multilateral organisations** do not have the flexibility or agility to work rapidly with different corporate partners

To overcome these limitations, it was necessary to create a new type of movement that was global and that engaged the world's best scientists, companies and test sites. This led to the birth of IAVI – a novel public private product development partnership – in 1996. IAVI's aim is to ensure the development of safe, effective, accessible preventive HIV vaccines, regardless of who develops the vaccine, or where. From IAVI's perspective, speed is the critical factor and industry's role is pivotal. IAVI aims to be pragmatic, flexible and most importantly, able to take R&D investment risks that private companies may not.

Progress and challenges

The world has made progress over the last decade, but many challenges remain. The world can, and must, do better. In this regard, one very important change is the growing involvement of the developing world in vaccine research. Trials are now taking place in six continents and in many developing countries (see Figure 1). However, several challenges need to be addressed:

- Although global spending on developing an AIDS vaccine has increased substantially, much of this money is still spent on basic research rather than product development
- The pipeline of vaccines being developed is narrowly focused, with a singular approach to solving the problem, and much unnecessary duplication
- The global capacity to hold large-scale trials is limited

- AIDS vaccines are still not a priority in terms of R&D spending, attracting less than 1 percent of all health R&D expenditure
- While several promising candidates are currently in trials, it is unclear whether these will ultimately succeed, and, if so, whether any of them will be effective in developing country populations

Figure 1

IAVI's work focuses on mitigating these challenges. By adopting a 'portfolio' approach to vaccine development and by working simultaneously with numerous corporate and public sector partners, IAVI hopes to maximise the chance of success (see Figure 2).

How can India contribute to this effort?

India's role in this regard is crucial. With a strong R&D capacity – and political support at the highest level – the country can, through public private partnerships, take a lead in developing an AIDS vaccine. Indian industry has developed expertise in other vaccines and enjoys a high level of technical sophistication. However, it has tended to concentrate on high-volume, low-value vaccines. In addition, average pharmaceutical R&D spending in the country is low – 1.9 percent of revenues, compared with 10-16 percent globally. Not surprisingly, India has yet to develop a fully novel vaccine. By improving the operating environment – through changes in the regulatory structure, ensuring TRIPS compliance and adopting policies that enable higher private investment – the government can help India move up the R&D 'value chain.'

A renewed global interest in vaccines makes this a promising area of work for Indian industry. The EU and G8 countries, the World Bank and regional development banks have all expressed their support for developing products that can be used in the developing world. The UK Chancellor, Gordon Brown, recently announced a £300 million fund for

purchasing malaria vaccines and similar support can be expected for an AIDS vaccine. Although the risks of developing an AIDS vaccine are high, the returns are also potentially very large. This, however, requires new R&D mechanisms, a pooling of global resources and effective public private partnerships.

Discussion

Question: What types of partnership models does IAVI adopt?
Answer: There are a range of different partnership models that can be adopted, depending upon the partner:

- **Independent or small-scale academic investigators**: Since the partner would have limited capabilities, IAVI would take the lead role in terms of contracting out R&D, manufacturing and process development
- **Small companies**: Joint product development would be an option in this case, with either side taking the lead on R&D
- **Large companies**: Here, IAVI's role would be one of an equal partner, with joint project management roles for IAVI and the large company
- **Multiple companies**: In some cases, IAVI has coordinated multiple 'pieces' of research from different companies, nations, etc.

Regardless of the partnership model adopted, an overriding concern for IAVI is to be able to ensure preferential vaccine access to those who need it most.

Question: What are IAVI's funding sources?
Answer: IAVI is supported by eight OECD governments, the EU, the World Bank and a set of private foundations and private companies.

Question: Would IAVI support multiple vaccine candidates from the same country? Since IAVI is already working with ICMR and NACO, would it be willing to also work with other organisations, and other vaccines, in India?
Answer: Yes, IAVI is willing to work with multiple partners. However, there are a few qualifiers to this. First, funding is limited, so it is not possible to support the entire gamut of basic science or early stage research. Second, IAVI works to identify the best ideas and to take these forward as quickly as possible. Third, IAVI, in conjunction with local partners like ICMR and NACO, tries to identify the strongest candidates – both internally and externally – and compare these with the existing world pipeline. If the candidate appears new and promising in comparison, it is more likely to get support from IAVI.

Comment (Seth Berkley): The government has set up a group within the ICMR to assess various candidates and to take these forward. This is the government's existing policy and one that will help streamline the process.

II. Session 2: The Industry Perspective

Mr Ranjit Shahani, Vice Chairman & Managing Director, Novartis India

Mr Shahani's presentation aimed to place HIV/AIDS within the context of other 'diseases of the poor' and within the world's overall socio-economic development framework.

AIDS and other 'neglected diseases'

HIV/AIDS is the single biggest threat to mankind today and one of the world's most severe healthcare crises. It is a global human tragedy that is reversing the development gains of the last thirty years. However, there are many other 'neglected diseases' and 'neglected populations' – and these are found disproportionately in the developing world. Very little research or funding is directed towards these problems – largely because their high level of localisation and their entrenchment in the developing world present few threats to developed countries. A number of additional factors impede R&D efforts in developing countries towards solving these problems, including:

- Poor infrastructure
- Inadequate monitoring and evaluation systems
- Limited government and donor funding and support

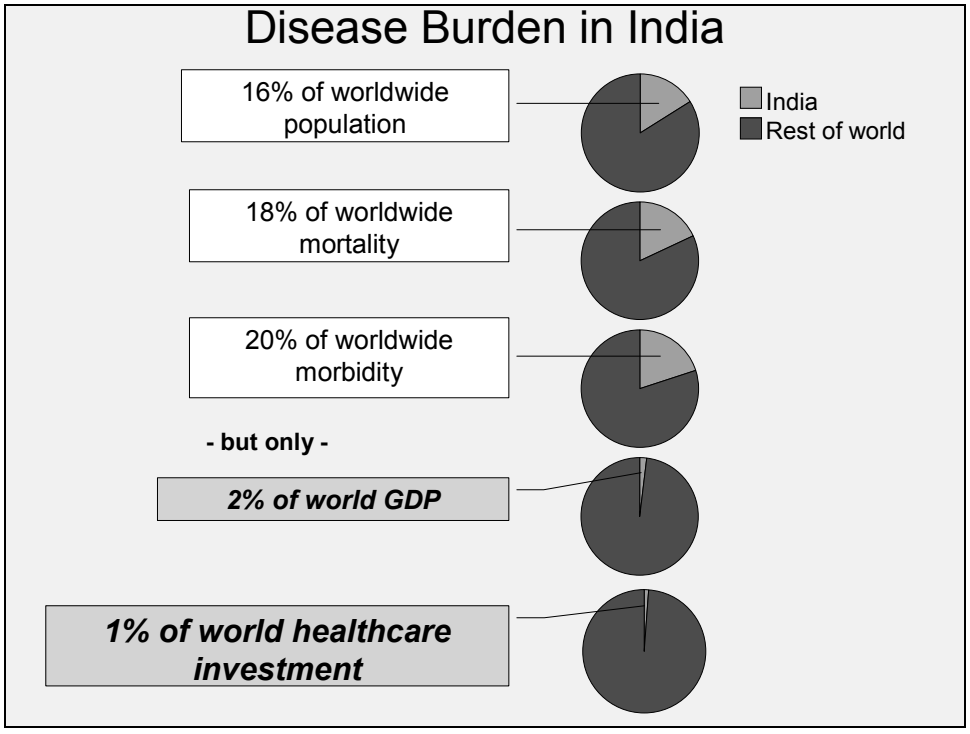
The socio-economic impact of AIDS

In addition to being a serious threat to human health, diseases such as AIDS create significant socio-economic problems. The incidence of HIV infection is highest in developing countries. As this disease tends to further impoverish the afflicted, HIV/AIDS threatens to widen welfare and lifestyle disparities and therefore exacerbate existing socio-economic problems. Ultimately this may have spill-over effects, including terrorism, which might also impact the developed world. At a national level, AIDS places an enormous socio-economic burden on the affected populations, and has, in some countries, drastically reduced average incomes and life expectancy.

A vicious cycle links poverty and the probability of infection (see Figure 2). Rates of infection are highest amongst the poor and diseases such as AIDS tend to progressively impoverish the affected – which raises the likelihood of new infections amongst the poor. Limited education and poor healthcare facilities make AIDS a massive challenge for developing countries like India – and this sustains the vicious cycle of poverty and infection. This cycle must be broken.

Turning to India, although the government had earlier aimed to achieve a zero level growth in infections by 2007, this, clearly, is not possible now. India has a disproportionately high disease burden, yet public spending on healthcare has averaged less than one percent of GDP (see Figure 3). The spending on prevention and treatment of HIV/AIDS is just 17 cents per capita. The new government has promised to raise this ratio to 2-3 percent of GDP – which is a welcome change.

Figure 2



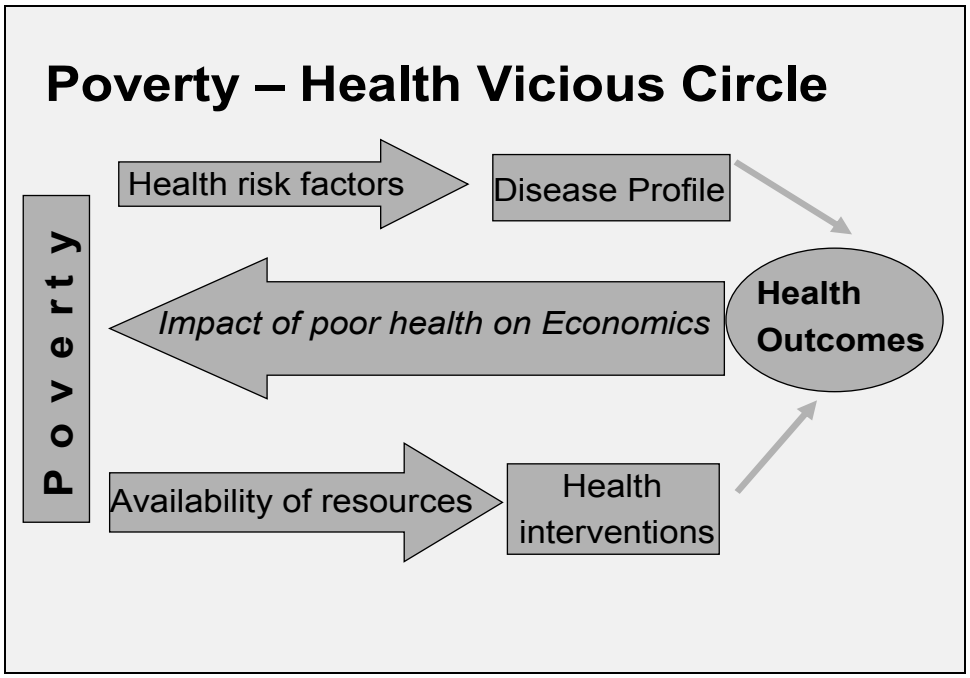
Overcoming barriers to research & development

In addition to low healthcare spending, a number of major barriers have impacted efforts to prevent and treat HIV/AIDS:

- Social stigma associated with the disease
- Poverty, illiteracy and poor sanitation
- Poor delivery systems and compliance
- The previous government's simplistic programmatic approach to the problem
- Limited cooperation between regulators and industry

India has great potential for vaccine research and public private partnerships are the key to unlocking this potential. These partnerships must be sustained, but to do so, much streamlining is required. India has one of the largest bases of intellectual capital in the world and this must be leveraged. For this, well-funded global public private partnerships are necessary, as is effective intellectual property rights (IPR) protection – which balances healthcare needs and national interest.

Figure 3



Above all, the ability to change certain aspects of the operating environment will determine the success of such ventures and of treatment and prevention programmes in general. Some important factors and possibilities for change include the following:

- **Awareness programmes** that leverage the reach of television and radio
- Strong **patent laws** to foster innovation and research
- A more **business-friendly environment**, to create opportunities for research, both national and global
- The development of a more **cooperative relationship between regulators and industry**
- **Effective partnerships** between research institutes, social organisations and NGOs
- The **streamlining of processes**, with regard to both HIV/AIDS and other 'neglected' diseases
- The mobilisation of **significant additional resources** to ensure effective delivery mechanisms

AIDS is a complex problem – an unprecedented crisis that requires an unprecedented response. A solution to this problem necessitates the mobilisation of the entire global public health community. In other words, what is required is solidarity between the healthy and the sick, between rich individuals and poor ones, and between the developed and the developing countries. Although the spotlight has been on the pharmaceutical industry, all stakeholders need to be involved in this effort.

Discussion

Question (Workshop Chair Kapil Sibal): What perception does the industry have towards this crisis? What can it do in terms of collaboration? How does it view the development of vaccines as a cure for HIV/AIDS, and how would it like government policy to respond?

Answer (by Mr Shahani): The honest reality is that industry has not fully woken up to this crisis. There are a few companies that are doing great work in terms of general vaccine development, but most firms are not fully accepting the scale of the HIV/AIDS problem. Education and communication need to be improved, as do distribution and delivery systems. Even if an effective vaccine is developed, it is necessary to ensure compliance and implementation. India's experience with tuberculosis – where compliance has been a major concern – demonstrates this. The central government can help by ensuring that an effective IPR regime is in place, but state governments will have to play a key role in implementing new models.

Comment (by a participant): There are no natural tools available to address the HIV problem and any vaccine would have to be a synthetic product. The technology required to develop a new molecule requires a large risk element, making it an extremely expensive proposition that is beyond the scope of industry's capacity. Indian industry's dominant role will therefore be to manufacture a product that, by means of economies of scale, would be cheaper to use.

Response (by the Workshop Chair): Industry appears not to be willing to contribute to developing the molecule. But, once it is discovered, industry hopes to produce the vaccine in bulk by exploiting the economies of scale. This is an old approach to the problem. AIDS is a global issue and industry needs to look at new models for developing partnerships between the private and public sectors, which will lead to increased R&D. Industry should tell the government what it wants – in terms of policy – to be able to do that, rather than to accept a second-rung role in this objective.

Comment (Vidur Kaushik, SRL Ranbaxy): As a reference lab, SRL Ranbaxy works in more than 350 cities in India and probably handles the largest number of AIDS patients on a monthly basis. One of its biggest concerns is the large gap between the quality of facilities available and government's system of managing patients. Today, for instance, industry is able to move samples anywhere within the country in six hours – a standard that is comparable to the best in the world. Yet, the state systems do not effectively use the available capacities. Another important issue is protocols with regard to clinical trials. Protocols need to be effectively managed, because there is a large gap between what the industry requires and what states practice.

Comment (Dr Sumedha Sahni, SRL Ranbaxy): A key factor that needs to be addressed is the sharing of information when it becomes available. There has to be some starting ground, or everyone will have to 'reinvent the wheel'. Industry has had experiences where information that is available with government agencies and laboratories – for instance, on new viral strains – is not shared. Without a system for exchanging data, industry will duplicate work that has already been done and in the process, waste resources.

Comment (by a participant): What India lacks is an enabling environment. If government and industry can create an enabling environment and reduce the barriers faced by researchers, global alliances become feasible. There are severe difficulties associated with importing technology or particular vectors. This makes it difficult for industry to collaborate with international partners. Steps should be taken to ease these constraints.

III. Session 3: Policy and Partnership Options in the Indian Context

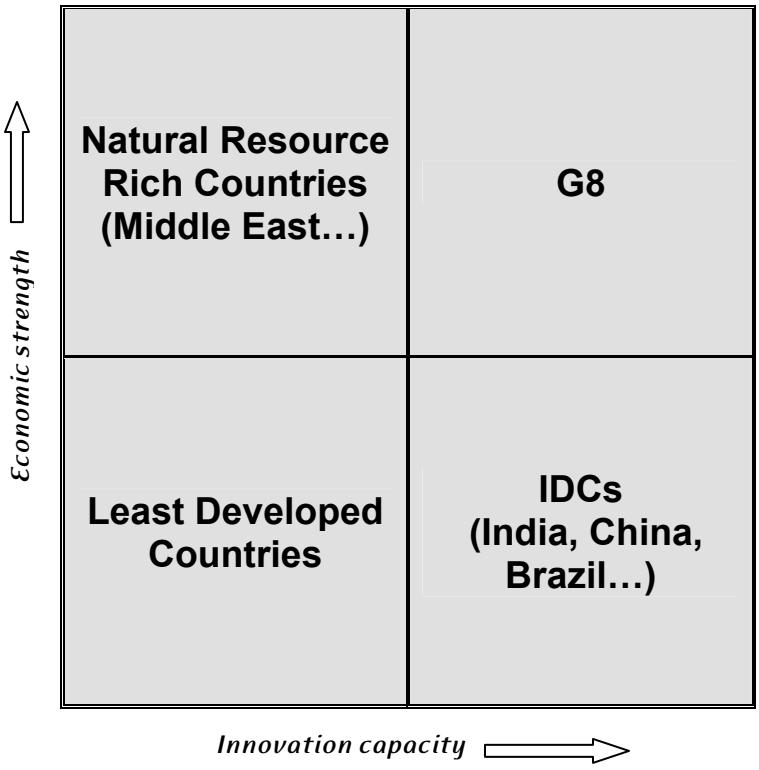
Dr RA Mashelkar, Director General & Secretary, Council of Scientific and Industrial Research (CSIR)

Dr Mashelkar provided a perspective on the important role of public private partnerships in research & development.

The role of Innovative Developing Countries

'Developing country' and 'developed country' are frequently used labels. However, some countries, such as Brazil, China and India, fall into a third category – of 'Innovative Developing Countries' (IDCs). These three nations, along with several other emerging economies, are starting to take a lead in drug research, development and manufacturing. Their role in overall scientific R&D, and in finding specific solutions – such as an AIDS vaccine – will be critical. Their importance can be measured by the fact that if IDCs did not exist, TRIPS would be a redundant issue.

Figure 4



IDCs successfully combine 'low economic strength' (relative to the industrialised world) with a 'high innovation capacity' (see Figure 4). This allows for high quality innovation at a relatively low cost. Rich countries, such as the US, still lead the world in such measures as the absolute number of patents filed, research published etc. The absolute contribution of IDCs is more modest. However, IDCs do relatively better when income levels are factored in.

To measure the true competitiveness of IDCs in research, it is useful to look at the ratio of academic citations to GDP per capita. Dividing the number of citations by average income, one obtains the following ranking:

1. India
2. China
3. United States
4. United Kingdom
5. South Korea

This is a very different ranking from one that compares the absolute number of citations. It suggests that an increase in funding per researcher in IDCs, and the number of researchers, will yield high levels of return, and increased competitiveness. The experience of CSIR in India – which has been steadily increasing the number of patents it has filed, and is now one of the top 10 filers of patents in the US – is evidence of this.

IDCs have the capacity to develop a competitive advantage in 'innovation' through five avenues:

- **Research and development**: leveraging the existing and potential high levels of 'intellectual capital per dollar' to achieve breakthroughs in research
- **Manufacturing**: the ability to produce large quantities at a relatively low cost – as demonstrated by India's bulk drug manufacturing successes
- **Export market development**: this requires cooperation from foreign countries, which can, and have, put in place barriers to IDC exports
- **IP management**: in this area, IDCs such as India have begun to establish strong IP protection mechanisms, but much remains to be done
- **Regulatory systems**: this is another area where IDCs will have to devote considerable effort, since the existing systems are neither transparent nor well-defined

The competitive advantage of IDCs will lie not in product-based **competition**, but in skill-based competition. Products have a transient nature that is dictated by the market. Skills, on the other hand, are permanent and allow countries and regions to continuously generate new ideas and products. The effect of this 'skill-based competition' is evident in the growing research clout of India and China.

Public Private Partnerships (PPPs) in India

Public private partnerships in research have worked well in India. Combined with India's manufacturing prowess, these PPPs can be of great value in combating global healthcare crises. For example, the Centre for Cellular Molecular Biology worked closely with Shanta Biotechnics to develop a recombinant DNA vaccine for Hepatitis B. When Shanta Biotechnics entered the market with this new vaccine (SmithKline Beecham plc already had an expensive, imported vaccine on the market), prices began to drop rapidly, eventually falling to less than five percent of the original price. In 2003, 10 million doses of the product were sold to UNICEF at approximately two percent of the original price. This – and the low scale of investments required to start and run successful biotech companies in India – demonstrates the potential for innovation in product development and manufacturing.

There is, however, a weak link between R&D spending and innovation. Although US pharmaceutical companies have greatly increased their research spending in recent years, the number of new chemical entities discovered has remained largely constant. This reflects a failure to identify unsuccessful candidates early on – which, by prolonging trials and research, significantly increases costs. IDCs have the capacity to leverage their research strengths to bring down the time and cost commitments associated with new product development. They offer three possible advantages to solve the problem of limited innovation relative to expenditure:

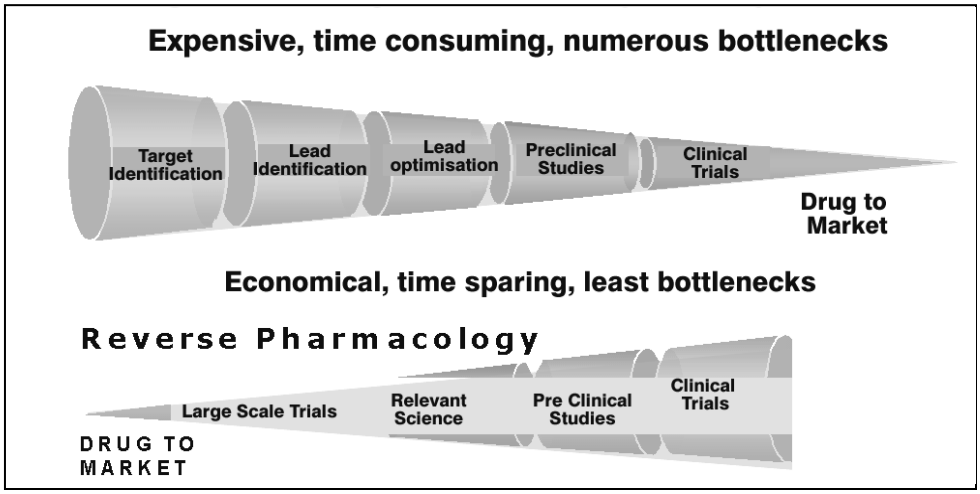
- **Low cost locations for R&D and manufacturing**: Here, IDCs can leverage their strengths in terms of:
    - Low costs per patient
    - Large pools of potential patients, leading to faster recruitment
    - Low costs per investigator
    - A strong base of Clinical Research Organisations (CROs)

- **'Smarter' science and technology**: Intelligent data mining can be used to obtain insights from existing data, which can reduce development costs. A large portion of current R&D expenditure, for example, pays for candidate failures due to liver toxicity. By intelligently using the existing (and vast) repository of invitron animal research to develop safer, cheaper models (e.g., predictive toxicology), such expenses can be brought down. India and other IDCs can develop non-clinical screening methods, including new statistical models, imaging technologies, etc., to better assess human risks, and therefore reduce costs.

- **Alternative paths of development**: Existing methods of product R&D do not always work. They involve long delays and large expenditures, which often result in failures. What is needed is the adoption of a 'reverse pharmacology' approach, which combines traditional medicine, modern medicine and modern science. Reverse pharmacology allows for reduced development time and reduced costs – and has been used in developing new responses to complicated diseases. (see Fig. 5)

However, it is necessary to put in place world-class regulatory systems to fully actualise these advantages.

Figure 5: Drug Discovery and Development Process



Successful examples from India

There is tremendous potential for successful PPPs in R&D in IDCs. A prime example of this is the CSIR's New Millennium Indian Technology Leadership Initiative (NMITLI). This consortium brings together 220 public institutions and private organisations. NMITLI has an annual budget of just US$ 10 million. However, by leveraging the strengths of its varied members (and by providing 'soft loans' that do not have to be paid back if an initiative fails), it has been able to achieve notable successes – including a bioinformatics software suite ('Biosuite'), and an early-stage breakthrough in the search for a low-cost treatment for psoriasis. Importantly, both of these breakthroughs came at a relatively low cost and required only short development times, as detailed below:

- Looking at Biosuite, small biotech companies would not individually have been able to afford developing such a product. On the other hand, universities and institutions that have the money have no experience with product development, while software firms lack the bioinformatics knowledge base on which to develop this product. By putting these three groups together at a relatively low cost and combining their strengths, a top quality product was created quickly and efficiently.

- In searching for a treatment for psoriasis, CSIR followed a 'reverse pharmacology' approach. Psoriasis is a complicated disease, afflicting approximately two percent of the world's population. At USD 20,000 per case, it is also very expensive to treat. The development of Amgen's anti-psoriasis drugs was an expensive and time-consuming process. In contrast, CSIR's research has yielded successful Phase I results at the cost of just US$ 4 million. If the final product proves successful, it would have taken just three years to develop, and will eventually cost just US$ 50 per treatment.

To sum up, global PPPs like IAVI can leverage the relative strengths of the rich countries as well as the IDCs. They must 'piggy back' on these strengths to find solutions. What are required most urgently are global partnerships to achieve global knowledge for global good using global funding. The current expenditure on healthcare research is miniscule and PPPs must seek to enhance this funding. They can do so by tapping a variety of sources – such as rich individuals and large corporations – not just in rich countries, but in the domestic market as well. There is no shortage of money, but it must be more effectively tapped.

Discussion

Comment: Industry has to play a key role in research and development. Since industry is able to focus on achieving results quickly even with limited funding, this capacity should be exploited through public private partnerships, where the public sector provides a large portion of the funding. Industry should be associated with R&D efforts from the start, even if its financial involvement is limited.

Comment: The traditional view that Indian industry can play a role in manufacturing vaccines, but not in developing new molecules, is passé. Today, several Indian pharmaceutical companies are developing new molecules which are in pre-clinical and clinical trials. Indian industry is capable of original research and must leverage these skills further.

IV. Session 4: Global Perspectives and Lessons for India

Dr Robert Hecht, Senior Vice President, Public Policy, IAVI

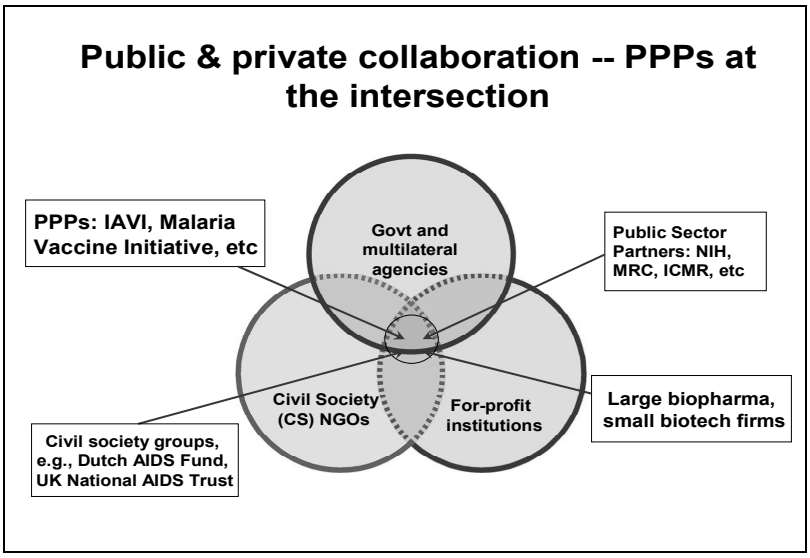
Dr Hecht's presentation focused on the issue of getting Indian companies involved in R&D towards an AIDS vaccine. In particular, he commented on the barriers and opportunities facing industry

Significance of PPPs.

PPPs are important because most R&D efforts focus primarily on diseases that affect rich countries (see Figure 6). Just one percent of the 1400 drugs approved by the FDA over the last two decades were for 'diseases of the poor', and less than one percent of NIH spending – a total of US$ 30 billion a year – is going towards these issues. PPPs help fill this gap by taking the best ideas forward as rapidly as possible. Further, PPP-oriented organisations like IAVI are prepared to take risks – by backing multiple candidates – in order to get results sooner.

PPPs are needed not just on the R&D side, but also to ensure rapid access to a vaccine when it emerges. Although a Hepatitis B vaccine was developed over 20 years ago, coverage rates in the developing world are still well below the levels needed to stop its spread. Thus, it is critical to plan, and act, far in advance to enable an AIDS vaccine to be effectively distributed.

Figure 6



IAVI's approach to partnerships

IAVI's PPP models are based on shared objectives. There is a sharing of risks, of decision-making processes and of the contributions and benefits for both sides. Typically, IAVI provides financing for the development of trial sites and for work towards access and distribution systems. Industry, on the other hand, provides the technology candidates, as well as know-how in terms of process development, clinical and lab practices,

manufacturing and project-management skills. Additionally, industry may also contribute financially and possibly provide for future manufacturing capacity.

In terms of financial returns, industry is usually offered the intellectual property and pricing rights for developed countries, while IAVI retains the right to provide low-cost access in developing countries. Some of the smaller biotechnology firms are provided with capital, which is often useful in 'kick-starting' their work. There may also be spill overs in terms of the development of technology platforms that can be used in other areas – such as other vaccines and drug development efforts.

IAVI's efforts are four-pronged:

- Research and development
- Product development
- Advocacy
- Public policy

One of IAVI's key roles is to advocate greater public spending on an AIDS vaccine, which is currently low in relation to the perceived needs.

Equally, it works to incentivise private spending on this effort, through public policy initiatives such as:

- Tax and fiscal measures
- Strengthening IPR regimes
- Advance purchase commitments

Advance purchase commitments are especially important because, since AIDS most visibly affects countries with the lowest ability to pay, firms do not have a clear assured market that will guarantee the recovery of R&D expenditures. Providing commitments to buy a certain quantity of a vaccine at a given price can encourage companies in this regard.

IAVI also works to overcome public policy and regulatory barriers that may be limiting the scope for product development. These efforts may include, for example:

- Establishing clear protocols that expedite the trials and approvals process
- Strengthening or establishing bioprocess capacities, especially for smaller firms and academic researchers that may encounter problems with scaling up

Enhancing India's role

How can India become more centrally involved and how can private companies play a more active role? IAVI would like to collaborate with Indian industry to form vaccine development partnerships by helping to put together the right combination of know-how, policies and an effective 'portfolio' of candidates.

The government, on its part, can help secure PPPs, increase the exchange of clinical information, create more effective regulatory processes and provide other incentives, such as IP protection, tax benefits and certain types of guaranteed payments. IAVI believes, further, that countries like India, China and Brazil can contribute to an advance purchase fund that would stimulate private sector spending in this sector.

Discussion

Question: How sustainable is IAVI's funding? Is it dependent on future revenue streams and what is its long-term strategy?
Answer: Although IAVI has long-term commitments from many different governments, diversification is critical. Clearly, IAVI would eventually like to generate a stream of revenue from its work. An AIDS vaccine will surely prove to be very profitable. However, the problem is that – given the controversies involved, such as whether it will be mandatory, questions about safety etc. – one cannot predict a timeline for cost recovery or profitability in advance. This is a challenge that IAVI will have to work with.

Question: If a company has an idea and has undertaken some preliminary research, at what stage should it come to IAVI for screening?
Answer: Typically, the more data the company has the better. However, it can come any time to ask for advice. This will help both IAVI and the company to evaluate the true potential of its research.

Question: How does IAVI maintain confidentiality when there are so many partners and conflicts of interest?
Answer (Dr Berkley): IAVI takes confidentiality very seriously. As IAVI has grown, the levels of due diligence and discretion have increased exponentially, but this remains a difficult issue. The more partners there are, the more difficult it is to maintain confidentiality. At the same time, the world is moving towards an environment of openness. There is a new movement of publishing all the clinical trial results, even negative ones. Also, journals do not accept papers unless they are finished ahead of time, so as to register trials etc. Thus, on the one hand, there is greater transparency, and on the other, one needs to worry about trade secrets, know-how and IP. PPPs like IAVI have to walk this line very carefully.

Comment (Dr Hecht): Although there are 25 or 30 different organisations that are involved in partnerships with IAVI, it is not one big mega partnership. IAVI has a number of different partnerships, typically involving two or three institutions alongside IAVI. Therefore, at least the ability to maintain a degree of trust and confidentiality is contained in that framework.

Question: What happens to the IPR that is generated before and after IAVI begins to work with its partners?
Answer: That depends on the agreements IAVI signs with companies and groups. Sometimes IAVI owns the IPR, sometimes the partner and sometimes it is shared. IAVI's only priority is to find effective vaccines.

Question: What is IAVI's stance on therapeutic vaccines?
Answer: There is obviously a huge market for therapeutic vaccines. However, there is no real precedent for such vaccines and IAVI has chosen not to make it a priority. This is partially because the greatest need is for a preventive vaccine. Further, everyone who is infected with HIV already has some damage to their immune system and testing a vaccine on such an individual can further damage their systems. Ultimately, AIDS is likely to be brought under control, not only with preventive vaccines but also with therapeutic ones. However, the primary target right now should be preventives.

VI. Concluding Remarks by Workshop Chair

Kapil Sibal, Honourable Minister of State for Science and Technology and Ocean Development

The government is thankful to IAVI for organising this initiative. It has provided an opportunity for industry, government and IAVI to openly discuss this issue. Five or seven years ago, such an open dialogue would not have been possible. Therefore, considering the scale of the problem, this meeting bodes well for the future.

IAVI represents the essence of what a PPP ought to be and this is the way to move forward. Industry today is more willing and perhaps a little more confident about the government's commitment to come forward and deal with this epidemic. On its part, the government believes that unless it provides incentives to industry and sets in place a regulatory mechanism that encourages investments in R&D in a much larger way, there will be little progress on this front.

From a commercial standpoint, industry stands to gain from investing in R&D towards an AIDS vaccine. This may not have been the case ten years ago. However, today, with the role of knowledge-based IDCs increasing, it is not enough for industry to simply provide delivery mechanisms and not to engage in R&D. This type of mindset must change. All stakeholders – academia, industry, government and NGOs – must play an important role going forward. Additionally, there must be a larger commitment from governments and international institutions than there is at the moment.

At the national level, it is necessary to put in place a more transparent and effective regulatory system. It is necessary to move fast, to find new methodologies and incentives. The government is willing to provide the requisite incentives, but financial incentives alone will not work. This is because the types of incentives governments can offer are miniscule compared to the risks that industry has to take. Therefore, incentives alone are not the answer.

What is needed is commitment. Essentially, there is a commitment that each stakeholder must make, because AIDS is not a local issue. This generation is dealing with the lives of future generations. Thus, commitment at the levels of industry, government, and the world community, are critical to finding a solution.

VII. Key Findings from the Workshop

Bringing together a diverse group of participants with similar objectives, the workshop was an important first step in promoting India's R&D efforts towards an AIDS vaccine. A number of broad lessons can be garnered from the presentations and from the subsequent discussions:

India can, and must, leverage its research strength to help find a solution. As a leading member of the 'Innovative Developing Country Club' – and as a country that has been seriously impacted by the virus – India is in a position where it can, and should, actively participate in the search for an AIDS vaccine. This will benefit India from a public health perspective, since the resulting vaccine will fight the strains of HIV that afflict this region. Further, Indian industry will gain both valuable experience in the process and develop an R&D infrastructure platform that can be used for research in related areas.

Industry, government and civil society are more willing than ever to collaborate on R&D. Perhaps the most important finding to emerge from this workshop is that government, industry and civil society organisations are now ready and willing to work closely together on creating an enabling environment and pursuing R&D ventures. A new level of openness and transparency has been established between these sectors and it appears likely that industry-government-NGO links will strengthen over time. This is apparent in the considerable success of such PPPs as CSIR's New Millennium Indian Technology Leadership Initiative (NMITLI).

PPPs hold the key to research and development of an AIDS vaccine. The large financial commitment required, the high risk of failure, and the lack of a large paying market for AIDS vaccines make it extremely difficult for the private sector to finance the entire effort on its own. This is especially true for companies in emerging markets, where finance is typically a critical limiting factor. Hence, it is imperative that PPP arrangements – along the lines of what IAVI has been doing – drive the global effort to develop a vaccine.

The private sector will, however, have to play a much more active role. While the public sector is good at basic research, the importance of the private sector's product development and project management skills cannot be emphasised enough. Across the world, most product development efforts have tended to originate in the private sector – and, in all likelihood, the same will hold true in the case of an AIDS vaccine. In India's case, while new product development is at a nascent stage, the private sector is rapidly gearing up to play a leading role going forward.

Government incentives are necessary, but not enough. Tax benefits, market guarantees and other such measures will help incentivise private sector investment by lowering the effective cost of R&D. More importantly, however, the government needs to **create an enabling environment** that will add impetus to the process. In the present context, R&D efforts are constrained by a number of factors, including:

- An IP regime that does not adequately protect innovators' property rights (improvements on this front, however, are to be expected, with a new patents regime coming into force on January 1, 2005)
- A regulatory environment that is short on transparency

- Poorly defined protocols for pre-clinical and clinical trials
- Inadequate information sharing across institutions, both private and public – which limits the speed at which new developments can occur
- A lack of institutionalised networking arrangements

State governments must play a complementary role. Although the centre can help create an enabling environment, it is the state governments that will have to implement systems and procedures to promote effective research. Private sector research efforts are being limited in part by shortcomings at the state and local levels – particularly with regard to protocols, the management of patients' needs, and the sharing of facilities and information. By addressing these shortcomings, state governments can directly and indirectly motivate this effort.

More money is needed for AIDS vaccine R&D, but existing funds can also be better utilised. There is little doubt that the global initiative to develop an AIDS vaccine will require significant financial commitments from governments and international organisations. However, it is not so much the size of the funding that matters, but how these funds are utilised. New partnership models, the effective use of existing data, and innovative approaches to the problem can significantly reduce R&D costs and lead times. This will help mitigate industry's earlier concerns with regard to the risk element.

Annex 1. Workshop Participants

Workshop Chair

Kapil Sibal, Honourable Minister of State (Independent Charge) for Science & Technology and Ocean Development

Speakers

Dr Seth Berkley, CEO & President, IAVI
Mr Ranjit Shahani, Vice Chairman & Managing Director, Novartis India Ltd
Dr Robert Hecht, Senior Vice President, Public Policy, IAVI
Dr RA Mashelkar, Director General & Secretary, Council of Scientific & Industrial Research (CSIR)

Participants

Mr Sumit Trivedi, Becton Dickinson India
Dr Subhra Lahiri, Biological E Ltd
Dr BM Khamar, Cadila Pharmaceuticals
Mr Swapan Bhattacharya, Chembiotek Research International
Dr RS Nadig, Eli Lilly & Co
Dr NY Sanglikar, Glaxo Smithkline
Dr JL Exceler, IAVI
Ms Anjali Nayyar, IAVI
Dr Queen Saxena, ICMR
Dr Dhananjay Patenkar, Intas Pharmaceuticals
Dr Ramani A Aiyer, Nicholas Piramal India Ltd
Mr Anil Kumar Chawla, Panacea Biotech
Mr Vijay Dahiya, Panacea Biotech
Dr VK Vinayak, Panacea Biotech
Dr Shoibal Mukherjee, Pfizer Ltd
Dr MS Mithyantha, Rallis India Ltd
Mr Bhaskar Malladi, Roche Scientific Co Pvt Ltd
Mr Vidur Kaushik, SRL Ranbaxy
Dr Sumedha Sahni, SRL Ranbaxy
Mr Sunil Kumar Bahl, Serum Institute of India
Dr SV Kapre, Serum Institute of India

IAVI (www.iavi.org) is a global not-for-profit organization whose mission is to ensure the development of safe, effective, accessible, preventive HIV vaccines for use throughout the world. IAVI's financial and in-kind supporters include the Bill & Melinda Gates, Rockefeller, Alfred P. Sloan and Starr foundations; the governments of Canada, Denmark, the European Union, Ireland, the Netherlands, Norway, Sweden, the United Kingdom and the United States; multilateral organizations such as the World Bank; corporate donors including BD (Becton, Dickinson & Co.), Continental Airlines and DHL; leading AIDS charities such as Crusaid, Deutsche AIDS Stiftung, and the Until There's A Cure Foundation; and other private donors such as the Phoebe W. Haas Charitable Trust B.

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