

Bio-business in brief: the case for ambitious action in the public sector[†]

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At the time of independence, India was a poor country. Nevertheless, the Government saw fit to invest in industry and research. In recent decades the public sector has received a bad press, with pressure to reduce it while increasing the role of the private sector. The public sector is not intrinsically bad, but has often been misused. The 'market' and the 'state' each have a role in economic development. To ensure steady growth of the economy, the country must ensure universal healthcare, for which it needs an innovative homegrown industry and universal good education. This requires large public investment.

Keywords: Basic research, biotech industry, liberalization, pharma industry, public sector.

LEADERSHIP is often about going into the unknown and making something happen, although the contours of the 'something' are not always clear at the outset. Sunil Khilnani's *The Idea of India*¹ reminds us that progress in the country after independence did not just happen. It took the leadership of the time to imagine what kind of country would be desirable, choose between competing visions and then take steps on many fronts. It behoves a country to have mechanisms to continually examine where it is and where it would like to be, from the near to the long term. As for other sectors, in the biomedical sector too, failure to do so has repercussions both for the individual and for the nation at large: millions of individuals will be condemned to avoidable ill health and premature death, and often, impoverishment. Furthermore, Amartya Sen tells us that there is no chicken-and-egg issue of good health and development: the former presages the latter, and one cannot wait for development to fund a broad-based health system that covers everyone². Even if the government has to borrow to fund certain fundamentally important public goods such as healthcare, this is acceptable under certain conditions³. The ensuing development fuels the economic growth that will help the government pay back what it has borrowed.

Looking back, it is clear that Jawaharlal Nehru and his colleagues took some remarkably independent-minded steps to develop the pharma industry in the country. But before discussing the industry, let us briefly discuss basic research.

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Basic research

Background

Even today, in the US, investments into basic research, for instance need to be defended. In a lucid piece, William Press⁴, addressing the members of the American Association for the Advancement of Science just a few years ago, provided several reasons for why basic research is required and why the investment of US\$ 40 billion by the government (3% of the Gross Domestic Product, or GDP) in basic research needs to be strongly defended. His various reasons included protecting people from hunger and disease, taking care of the environment, deterring or winning wars, and providing an outlet for the talent and imagination of young people. He goes on to describe how technology (which arises from basic scientific advances) is a 'factor of production' like capital, land and manpower, except that it generates more of itself. In that sense it is a very powerful factor of production, and technologically strong nations tend to have strong economies. Also, the most advanced nations have all invested around 3% of their GDP in basic research, and understand that it is a long-term game with unanticipated spin-offs along the way.

GS: As Secretary, Department of Biotechnology, Government of India, on several occasions you have mentioned the need to further strengthen basic research in the country. I am sure that you agree with Press' thesis?

KVR: I think there has been, in recent times, a false debate between basic and applied research. There are two separate questions for a country such as India. First, how much should we invest in research? The second is, how do we benefit from research to solve a variety of problems

and create new applications? When we conflate these two questions, we run in circles and head nowhere.

Investment in research is investment for the future. All of today's applications are the result of past investment in research. The West made much of this investment, but India benefits from its post-independence investment too. The rising Indian biotech industry owes much to the country's investments in chemistry and structural biology. So, if we want to become a truly innovative knowledge economy in the future, we must invest in research today. For some of today's applications, we use the fruits of research investment from anywhere in the world. But for other applications, solutions can only come from research done in India. If we substantially purchase the fruits of research done elsewhere we will become a vassal state, and even then we will not find solutions to our problems.

There is no such thing as basic or applied research. There is excellent, good, bad and meaningless research. Excellent researchers, as a community, will always address top-quality problems, already defined by the best in the world and be globally noticed; or they will define top-class problems themselves, by looking around them, and will lead the world in solving them. These problems could be basic or applied. Funding agencies love to work with such researchers and formulate innovative calls for proposals. Good researchers are those who do a good job at problems defined by others. At the least, good researchers train those who may become excellent researchers. They are not to be sniffed at. Most of the best in India are good researchers, admired by others in the West for the quality of their work and their training, but are not viewed as serious competition globally. If Indian researchers are to be seriously competitive, one way is that we look around us and solve major questions that are inspired by the complexity of our environment. The life sciences, in particular, afford this opportunity, in areas such as animal (including human) biology, disease biology, ecology, evolutionary biology, biomaterials, marine biology and so on. These areas require a huge stimulus of research support, but importantly, an inspired frontier spirit that attracts the best from all over the world, of any nationality, to India. Immigrants aided the transformation of American post-war science in no small way. The five Martians (Leo Szilard, John von Neumann, Theodor von Karman, Norbert Weiner and Edward Teller), so called because they were so extraordinarily brilliant that people joked that they must be from Mars, are an example. Each working in his driven ways did extraordinary basic and applied research that changed America and the world. Today, India can inspire the best in the world to come here, and lead a peaceful transformation through research in biology. Asia and Africa offer a treasure-box of problems anchored in biology that make for the best in basic and applied biology. Addressing

these problems will put these continents in the forefront of research, which will provide truly inspirational solutions to pressing problems that the planet faces. Countries such as India can and should take the leadership in the formation of, for example, an Afro-Asian Scientific Union, that combines the features of both the European Molecular Biology Laboratory (EMBL) and the European Molecular Biology Organization (EMBO). Such a Union could create a fund and mechanism that allows the best of any nationality to work in laboratories in the region. Developing and nurturing local talent is a must and combining this with international links allows us to grow exponentially rather than linearly. If America had kept aliens (such as the five Martians) out, it would still be a place with a future, not a place which shapes the future.

In sum, we must invest in research; to develop it is a part of our character. Strange as it may seem, this requires us to open our doors wide, so the best can come and go through our intellectual gardens. If we do this well in the next five years, we will see a transformation. This rapid transformation is possible because we have, due to the past 70 years of investment, an excellent collection of quality parts. As the winds from the world waft through our open doors, the parts will come together and the resulting cooperativity will be rapidly transformative. This is the way rapid change took place in the United States.

GS: One could perhaps add two more points about good scientists. First, as someone once remarked, the country must have familiarity with the various sub-domains of science, just to be able to resist any external power trying to bamboozle us in those areas. A high order of 'literacy' in a sense. Second, a techno-entrepreneur should be able to access the knowledge of a scientist in his/her area of interest. A scientist does not need to be outstanding to be useful to the entrepreneur.

KVR: Yes.

GS: While on the topic of basic research, about 15 years ago, an editorial in this journal⁵ regretted the fact that a non-resident Indian had to be brought back to head the Tata Institute of Fundamental Research, Mumbai due to a 'missing generation' of potential leaders. The situation may not be radically different today, and even highly accomplished senior scientists from abroad may not transplant well. What do you think is the solution?

KVR: I do not think we should focus solely on local leadership. A bit like a gold rush, one could have scientific leadership from anywhere in the world who come to India for some years. The kind of infrastructure and processes, etc. that they help build would be extremely valuable, with the gold almost becoming irrelevant. So, for instance, if we could get 10 of such leaders each year for 10 years, that could transform the landscape.

The evolution of the Indian pharma industry

Background

To return to the industry, whereas in 1947 the Indian pharma industry was worth Rs 10 crore, in 2009–10, it was worth Rs 1 lakh crore⁶ and in 2016 it was worth double that value (<https://www.ibef.org/industry/pharmaceutical-india.aspx>). Most of the industry from independence till the 1960s was dominated by multinationals; in 1970, multinationals had 80–90% of the market, and largely imported the bulk chemicals and formulated them in the country⁶. A US Senator, Estes Kafeveur, commented at the time that drug prices in India were amongst the highest in the world⁶. By 1999, Indian companies had 61% of the local market⁷. By 2007, India was a world leader in high-quality generic drugs, producing 20–22% of the world's supply⁸. One of the early steps that enabled this transformation included the setting up of the public sector Indian Drugs and Pharmaceuticals Limited (IDPL) with help from the erstwhile Soviet Union. When that did not result in lower drug prices, further measures were enacted in the 1970s⁶: (a) the Indian Patent Act of 1970 that disregarded product patents, thereby allowing a 'copying' of on-patent drugs provided the synthesis was by a different process; (b) successive Drug Price Control orders from 1970 onwards; (c) production controls, with different drugs reserved for the small scale or the public sector, or which the multinational companies could also produce⁹; and (d) the prohibition of Foreign Direct Investment (FDI) and increased tariffs on imported drugs⁸. In parallel, there was the setting up of universities and Council for Scientific and Industrial Research (CSIR) labs; and, in fact, IDPL and the Indian Institute of Chemical Technology (then known as the Regional Research Laboratory), for instance, were located in the same city and had much to do with each other¹⁰. Each of the examples above highlight the role of the state in creating enabling conditions for domestic industry. In a lucid and interesting book published in 1996, just a few years after liberalization, Bhaduri and Nayyar³ talk about how industry and the market can never flourish without the enabling hand of the state. The market and the state must co-exist, and must play different but complementary roles that evolve with time. Neither is intrinsically better or worse than the other.

What the Indian industry has achieved over the past few decades has been remarkable. But if it has to get to the next level, it must – *inter alia* – discover new drugs. Even as recently as 2012, new drug discovery has been considered an elusive goal⁶, although there have been a handful of efforts, earlier amongst the large generics firms¹¹ and now even amongst start-ups¹².

GS: From your vantage point, do you feel that industry is not doing certain things?

KVR: Industry has had a tendency to look for immediate monetary gains. There has also been some unhappiness over the lack of involvement from Indian academia. However, it is possible for industry to engage with academia or non-profits or governments anywhere in the world. India needs solutions to huge problems, at a huge scale, and industry could get the requisite monetary gains by providing these solutions. Just like the mobile phones, that were much needed.

GS: In the 1970s, the cars on India's roads were clunky, but at least they were made here. Many other developing countries simply imported the fanciest cars in the world. Today, we produce better cars. It has taken decades, and it is not clear that this could have been hastened infinitely. I am sure that if it took decades to produce good cars, it could take longer to produce good drugs, and therefore we need to start the process soon.

KVR: Yes, and we do have good examples of people trying very innovative approaches to drug discovery. This is another area where I feel it is not difficult to have exponential growth in the efforts in the country.

GS: After the financial crisis in the US around 2008, there were reports of many small biotech companies being in danger of going under because they just had a few months' worth of cash in hand¹³. Normally they would have to reach a certain milestone before raising another round of venture capital. It seemed to me that this was a 'garage sale' situation, where it should be possible for Indian companies, for instance, to pick up great bargains in terms of research and development (R&D) capabilities (which would come lock, stock and barrel, i.e. the people, the assets, the scientific advisory board, etc.). As far as I know, not a single Indian company did so. At that point I used to go around asking people why Indian companies were not buying these biotechs. Most people had no answer. But then one or two of them said 'Because they are not comfortable handling R&D'.

KVR: Yes, but that situation is changing, and that change could be accelerated.

The public sector

Background

Let us go back further in time. A then-famous but subsequently forgotten plan for the economic development of free India was brought out by a set of prominent Indian businessmen in 1944 and 1945 (ref. 14). This document came to be called The Bombay Plan. With the examples of industrial development in the Soviet Union and Germany, the industrialists acknowledged the need for state intervention to speed up industrialization. The Plan called

for the building of fundamental industries such as steel, heavy machinery, chemicals, power and fuel to be developed by the government in state-owned or controlled entities, with other sectors left to private industry. As it turned out, conditions in the few years after independence were far tougher than had been anticipated: with the loss of wheat-growing lands to Pakistan, money had to be spent to import food; large amounts had to be spent on settling displaced people; the war-time economy (related to the Second World War) had ceased to exist; the tax base was low and people were not saving at the rate assumed in the Plan¹⁴. Nevertheless, the government of this highly impoverished country whose GPD was largely from agriculture saw the imperative and found ways to promote R&D, and this plan was actually closely mirrored in the first few Five-Year Plans. India was not alone in this: many countries attaining freedom around that time looking both to the largely comfortable lives in the West and to how colonial rule had prevented their development, felt that industrialization was key to helping lift their countries out of poverty¹⁵. That is, they had to play 'catch up' with more industrialized countries. It is interesting to note that in those impoverished and difficult days, the government saw fit to make such large investments, whose benefit the country has reaped in subsequent decades.

The why's and wherefore's of economic development are, of course, of central interest to economists. Nayar's¹⁶ book of a few years ago, has looked at the economies of different regions of the world over the centuries. He makes the interesting point that only about 14 developing countries are really important, with high GDP or GDP/person, as countries that are rapidly catching up with the developed countries today, although another 10–12 countries could join their ranks. This is a very small number, and he asks why these particular countries. Many of them are not democracies and many also score high on corruption; so these factors cannot be critical to economic growth. He does find, though, that the initial conditions, including a history of manufacturing, suitable enabling institutions and the 'hand of the state' play a crucial role. He also stresses the importance of 'bridging institutions between academia and industry'. If there is a country with good 'initial conditions' for another forward leap, it is surely India. Perhaps it was a more equivocal situation in 1947, but the country has invested wisely on many fronts, both in the private and public sector, and there is certainly a base for new kinds of efforts. Bhaduri and Nayar³ in their book also talk about how foreign investment will happen only once certain infrastructure is in place. This could be soft infrastructure like qualified human resources, or physical infrastructure like good roads, both of which bring down the cost of doing business. International capital can move around the world very easily, and if it is to be attracted, the conditions for its productive deployment have to be provided. There are

certain things the state must do the heavy lifting on, although the private sector can complement it.

To give a fairly recent example of public sector action, after India's successful launch of a probe to Mars, an engineer is quoted as saying that he had slept at the satellite centre almost each night for the previous 15 months¹⁷. Although the public sector has received a bad press in India for the last couple of decades, the statement above reminds us not only that there are hugely dedicated professionals working in this sector, but also that with clear goals, good leadership and consistent funding, there have been stunning accomplishments. Bhaduri and Nayar³ stress that there is nothing intrinsic to the 'public' nature of the public sector that makes it inefficient. It is the misuse of and interference in the sector that have caused it to under-perform and acquire a bad name. The Indian Space Research Organization is a good example of a public sector institution that has performed.

GS: In the early years, Nehru made a distinction between the Bhakra and Nangal dams which he was willing to let engineers from abroad take care of, and the manufacturing of antibiotics in which he favoured an arrangement that involved the concomitant setting up of a research unit¹⁸. Do you believe that we need to make similar distinctions today? Items that can be left to the private sector, versus those that need to be supported by the public sector, at least for now, so that the country's capabilities develop stronger and faster? Bhaduri and Nayar³ talk about the importance of this in their book too.

KVR: This is an important distinction. In principle we could say 'Why not ask industry to take care of the functions of the army or the police?' So, one company could handle a Kargil-type situation and another company could handle another problem somewhere else – they could bring in mercenaries from anywhere in the world and the government would pay for it. Well, of course, we cannot do this. It is the government's commitment to its people that it will take care of the boundaries of the country. We need to extrapolate from this – the government has to show a commitment to its people on various fronts and cannot outsource things. Of course, how it does this may vary with the case. So, it has to run the railways to cater to the entire population, but it could certainly outsource the catering or building the coaches or some other aspect. Or, it could own only 20% of some service that it currently owns 100% of, but bears moral responsibility for offering that service.

We also have to remember that things can be debated endlessly, but this is not without consequence. If we do not vaccinate, hundreds of thousands of people will die. But we get caught up in debates about vaccines and pricing strategy of the private sector, etc. If public sector manufacturing has failed in some instances, can we not find out why that happened and correct it?

GS: A few months ago, the Union Cabinet approved a five-year Rs 1500 crore programme – that will be funded by the central government with half the funding from the World Bank – that will support product development in the biopharma sector (<http://pib.nic.in/newsite/PrintRelease.aspx?relid=161877>). This step mirrors some of the thoughts in this article very closely, and should lead to considerable progress on many fronts.

KVR: Yes.

GS: Economists have commented on how, given World Trade Organization (WTO) rulings, India has much less room for manoeuvrability today than it did in the 1970s, and ‘public spending’ and ‘subsidy’ are often treated as bad words. Do you agree?

KVR: These are political games. One cannot push too hard in one direction, because one could be squeezed in another. On the other hand, as the Indian industry grows bigger and stronger, it will be able to drive bigger bargains. Or, as the economy grows stronger, the country as a whole will be in a stronger bargaining position.

GS: Healthcare and education are two fundamentals that the country must get right. Every industrialized country – including those that have industrialized recently – has taken care of these two things. Would you like to comment on education?

KVR: I would like to make two points:

First, India is sitting on a demographic bomb. A few hundred million young people are going to want higher education and jobs in just a few years. Let us say that the government gave 10,000 scheduled caste/scheduled tribe students scholarships to study anywhere in the world, provided they got admission in those institutions. Let us also assume that the government subsidized their preparation for these exams through any coaching centre in the country. Within 5–10 years, there would be a transformation in the quality of these education students, and in the leadership in this community. The same formula could be applied to the North East, Kashmir, or any other group. Yes, there will be a cost, but there will also be a big cost to not doing something.

Second, I think it is very important that science is taught in both English and in the students’ mother tongues. Right now only urban youngsters have access to science, since it is almost invariably taught in English. We are losing a lot of talent due to this.

GS: And translations from English need to be done carefully. I have heard that sometimes this is not the case, and students end up reading gibberish in their mother tongue.

In summary, we have argued for the need for ambitious public action in the sciences and in educating youth from disadvantaged communities and regions. No country has progressed without this. Fundamentals like this cannot be left to the market.

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