Biotechnology and Development Monitor
No. 25, December 1995

Vaccine Policy in India

By
Sachin Chaturvedi and Beena Pandey

Keywords: India; Vaccines (human); Policies/Programmes.
Correct citation: Chaturvedi, S. and Pandey, B. (1995), "Vaccine Policy in India." *Biotechnology and Development Monitor*, No. 25, p. 5-7.

The Indian *Department of Biotechnology* (DBT) has initiated several R&D projects for the development of improved vaccines and immunodiagnostics. These vaccines could replace poorly performing conventional ones, or broaden their target range of communicable diseases. The emphasis is on the build-up of a domestic capability in R&D and vaccine production.

The lack of an effective health care system in India is especially acute due to the high incidence of communicable diseases. Between 1988-93, under 5 year mortality rate in India was 122 per 1000 live births, or an estimated 3 million Indian children die under the age of five each year, while an equal number become disabled due to diseases. Despite huge investments in health care, public institutes have yet to make significant contributions to meet India's requirement for modern vaccines.

Health care policy

Over the last two decades, mass immunization of children has been the primary objective of India's public health care system to prevent the spread of infectious diseases. The most significant initiative in this respect was the *Expanded Programme of Immunization* (EPI) introduced in 1978 against three of the most common diseases affecting children: polio, tetanus and diphtheria. Subsequently, vaccines against measles and hepatitis B were also included in the Programme.

Preventive health care, of which the importance was emphasized by the EPI, became the focal point of the *National Health Policy* adopted by the Government in 1982. This Health Policy reflected India's commitment to the international goal agreed upon

in Alma Alta: 'Health for All by the year 2000.' The Policy enlarged the scope of preventive health care by re-emphasizing the need to control additional major communicable diseases like tuberculosis, leprosy, diarrhoeal diseases, malaria and filaria.

Central to the Policy was the objective of providing protection, illustrated by the expansion of the EPI into the *Universal Immunization Programme* (UIP) in 1985, which aimed at providing coverage of immunization to pregnant mothers and infants. The UIP was adopted as a 'Technology Mission'. It was designed as an end-to-end programme, i.e. to promote, set up, undertake and monitor highly competitive R&D activities in vaccinology, and to achieve self-sufficiency in vaccine production. Under the Technology Mission, the DBT was entrusted with: (1) the production of vaccines hitherto not produced in the country; and (2) R&D for new and improved vaccines. DBT has set up three expert/technical committees in 1988 to evaluate the state-of-the-art technologies for the production of oral polio vaccines (OPV), inactivated polio vaccine (IPV) and vaccines against measles and rabies. For the production of IPV and rabies vaccine, the committees opted for the Vero cell (micro-carrier) fermentation technology; for production of the measles vaccine they chose the chick embryo fibroblast cell culture technology; and for OPV the committees selected primary monkey kidney cell culture based technology.

India's vaccine production and demand

The Indian vaccine market is growing at a rate of 8 to 10 per cent per annum, but the country is still spending US$ 12 million on imports of primary vaccines. In 1993, the total turnover of Indian production of human vaccines at manufacturers level was around US$ 33 million.

Currently, India depends on domestic production in the case of DPT (diphtheria/ pertussis/ tetanus booster), DT (diphteria/tetanus booster), tetanus and BCG (anti-tuberculosis) vaccines. The estimated demand of oral polio vaccines is mainly satisfied by imports. For some of the other major diseases like typhoid and hepatitis B, domestic production is negligible, while imports meet only a proportion of the demand (see table on page 7).

The whole cell cholera (as also in other parts of the world) and typhoid vaccines which were produced and used in India, performed so poorly that mass immunization with these vaccines was discontinued. DBT has also identified the pertussis component of the DPT vaccine as of low efficacy and highly reactogenic. An improved pertussis component, like an acellular (sub-unit) vaccine which is in an advanced stage of clinical trials, would reduce the number of doses (currently 3)

required for DPT. The BCG vaccine that is currently used worldwide is also of doubtful efficacy. It calls for urgent efforts to improve this vaccine, since tuberculosis is still the number one killing disease in India, according to a *World Health Organization* (WHO) report.

Recently the Government of India has taken some initiatives to promote domestic production of vaccines. The *New Drug Policy* of 1994, for example, states that the genetically engineered drugs produced by recombinant DNA technology and specific cell/tissue culture targeted drug formulations will not be under price control for five years from the date of manufacturing in India.

With public sector failing to meet the expected advancements in production and technology development, the lifting of the price control aims at attracting private sector to invest in these areas. Although foreign investment in the production of drugs using recombinant DNA is not automatically approved, it is recognized that foreign subsidiaries are important since their production in many vaccines exceeds the production by public institutes. Therefore, there is a need to restrict the list of vaccines reserved for the public sector to only a few vaccines in which heavy public investment has been made and for which the capacity in the public sector is adequate to meet India's demand.

Public sector institutes

There are many public sector institutes which develop and produce vaccines under the control of central or state governments. Both conventional techniques and modern biotechnology are deployed. For example, the leading *Central Research Institute*, Kasauli, Himachal Pradesh, has developed vaccines against DPT, DT, tetanus, cholera and typhoid through fermenter and other conventional techniques.

Similarly, the BCG *Laboratory*, Quindy, Madras, has successfully produced the BCG vaccine.
The *National Institute of Immunology* (NII), New Delhi, is one of the premier research institutes in India applying biotechnology for vaccine development. It has worked extensively on research and development of an anti-fertility vaccine (see also the article by Sprenger). Trials at the *All India Institute of Medical Science*(AIIMS), the Post Graduate Institute of Medical Sciences and Safdarjung Hospital in New Delhi were considered successful. The *International Centre for Genetic Engineering and Biotechnology* (ICGEB), New Delhi, has initiated the production of a recombinant version of this vaccine.

Private sector involvement

Indian private companies have largely focused on high-priced vaccines, which is reflected in their research priorities. Hepatitis B, MMR (measles/mumps/ rubella booster) and oral typhoid vaccines have attracted their attention. *Hoechst India* and *Cadila* have focused on development and import of oral and injectable vaccine against typhoid. Hoechst India is also producing a rabies vaccine. Cadila has a genetically engineered vaccine against hepatitis B in an advanced stage of laboratory development.

Another division of the Cadila group, *Alidac*, is importing and marketing an anti-rabies vaccine. *Glaxo, Biological Evans Ltd*., and*Serum Institute of India* account for a large share of Indian DTP production. Some relatively new firms like *Panacea Biotech* and *Shantha Biotech* have also taken up R&D work on hepatitis B and oral polio vaccine.

Most of the pharmaceutical companies are not open about their research plans. The secrecy surrounding drug development is indicative of the awareness of the expected changes in India's patent regime by the year 2000. Since India has accepted the Uruguay Round Agreements, it is committed to change the process patent regime hitherto prevailing in the country into a product patent regime. Consequently, in the future Indian companies have to come up with novel products to survive in an increasingly competitive market, instead of basing their expansion on the development of new processes, as they did in the past.

Requirement, production and import of important vaccines in India

(in million doses)

	Requirement		**Production**		**Import**	
	1994-95	**1999-2000**	**1985-86**	**1994-95**	**1985-86**	**1994-95**
DTP	105	114			Nil	Nil
DT	50	57	71	97	0	0
Tetanus	75	200	28.3	45	0	0
BCG	41	24.3	54.9	75	0	0
Oral Polio	105	134	17.8	10	17.8	90
Measles	42	46	Nil	Nil	Nil	Nil
MMR	5	7.5	3.8	23	?	0.1
Rabies			?	4.5		
-sheep brain	1	1.5			0	Nil
-cell cultured	3	5	Nil	4.5	0	1
Hepatitis B			Nil	1.0		
-plasma derived	0.1	0.2			?	0.07
-recombinant	1	45*	Nil	Nil	Nil	0.3

Typhoid	10	50*	0	0	0	1
H. influenza type B	1	5	0	0	0	Nil
Meningitis	0.5	2	0	0	0	0
			0	0		

D: diphtheria; T: tetanus; P: pertussis; MMR: measles/mumps/rubella.
* If included in the EPI vaccination programme, demand may multiply.

Source: Based on personal communication with Dr. P.K. Ghosh, Department of Biotechnology, Government of India.

Collaborative efforts

The DBT has been producing several vaccines in collaboration with many developed and developing countries. The main objectives are to share knowledge with other countries on recent developments in vaccines, training and exchange of information and scientists. India's ongoing vaccine projects have been carried out in cooperation with USA, Belgium, Germany, France and Russia. New initiatives have been taken or planned with *South Asian Association for Regional Cooperation* (SAARC) member countries (including Bangladesh, Bhutan, India, Nepal, Pakistan, Sri Lanka and Maldives), Poland and China.

With China, for example, the DBT has proposed to collaborate in the development of diagnostics and vaccines against hepatitis A, B, C, and E. Earlier in 1987, the DBT initiated the *Indo-US Vaccine Action Programme* (VAP), a joint bilateral programme on applied research and development of vaccines and immunodiagnostics. The *Joint Working Group* (JWG), which was constituted by the two governments, identified viral hepatitis, rotavirus, cholera, E. coli, typhoid, pertussis, Pneumococcus, Haemophillus influenza, canine rabies, respiratory syncytial virus, and polio as priorities for collaborative research under the Indo-US VAP. The JWG also reviews the progress of implementation of VAP in both countries. In addition, two projects on typhoid vaccine evaluation were authorized at AIIMS, New Delhi and at the *Tuberculosis Research Centre* (TRC), Madras.

In 1989, the DBT jointly with the *Ministry of Health and Family Welfare* established *Bharat Immunological and Biological Corporation Ltd.* (BIBCOL) in Bulandshahar as a production and R&D unit for production of human viral vaccines. Among others, BIBCOL was established to manufacture 100 million doses of oral polio vaccines. The main process building has been designed according to all WHO requirements of Good Manufacturing Practices, for the first

time in India. A continuous tunnel with vial washing, sterilizing, filling and labelling system, with a capacity of 6,000 doses per hour has been imported from Germany. Initially, BIBCOL has imported bulk oral polio vaccines from SKF, Belgium for the manufacturing of individual doses. It was planned to release the vaccine after a quality control through the immunization programme in mid-1995, but this is likely to be delayed.

Another *institute Indian Vaccines Corporation Ltd*. (IVCOL), Gurgaon, was incorporated as a joint venture of the DBT, *Indian Petrochemicals Corporation Ltd.* (IPCL) and *Pasteur Merieux Serums and Vaccinnes* (PMSV), France, the three organizations equally sharing the equity capital. Initially, IVCOL was to produce measles vaccine, Vero cell based inactivated polio vaccine and rabies vaccine. The inactivated polio vaccine lost its priority when in 1991-92 the WHO directed the Ministry of Health and Family Welfare to use only oral vaccines for polio control in India.

Therefore a joint Indo-French committee reviewed the 'product mix'. At present DBT is exploring the possibilities for domestic oral polio, measles and rabies vaccine production by using Vero cell based micro carrier fermentation technology from PMSV. Negotiations for the transfer of technology have already been started with PMSV.

Sachin Chaturvedi/Beena Pandey**

**Research and Information System for the Non-Aligned and Other Developing Countries, Zone IV, Fourth Floor, India Habitat Centre, Lodhi Road, New Delhi 110 003, India. Phone (+91) 11 4617 136; Fax (+91) 11 4628 068.*

Sources

Government of India (1995), *Economic Survey* 1994-95. New Delhi: GOI, Ministry of Finance, Economic Division.

Department of Biotechnology, *Annual Report* 1987-88, 1994-95. New Delhi: GOI, Department of Biotechnology.

P.K. Ghosh (1993), "*Biotechnology in India." Australasian Biotechnology*, 3 (4), August, pp. 214-222.

P.K. Ghosh (1995), *Biotech Industry Guide*. New Delhi: BCIL.

T.S. Rao (1994), "Current Trends in Vaccine Development: Beyond ifs and buts." *Journal of Basic and Applied Biomedicine*, 2 (1), 67-69.

World Bank (1995), *Social Indicators of Development*, 1995. World Bank.

Personal communications with *Dr. Niraj Arora*, IVCOL, New Delhi; *Dr. S.M. Saxena*, BIBCOL; *Dr. Jotna Sokhey*, Ministry of Health; *Dr. M.S. Negi*, PMSV;*Dr. R. Venkataraman*, Hoechst India; and *Dr. P. Gupta*, CRI, Kasauli.