Meeting Local Needs in Global Times
Case of Universal Vaccines in India

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Abstract: *This article analyses access to stable and affordable supply of vaccines that are needed for mass immunisation programmes, during the post liberalisation period and new IPR regimes. The article points out that the Indian experience of sudden shift from public sector to private sector and preference to public private partnership models at the cost of public sector has not ensured access to universal vaccines to Indian children. The lack of good governance, strict regulation and an evidence-based rational national vaccine policy are major stumbling blocks on the road to a sustainable, affordable stable universal vaccine supply in India.*

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I
Introduction

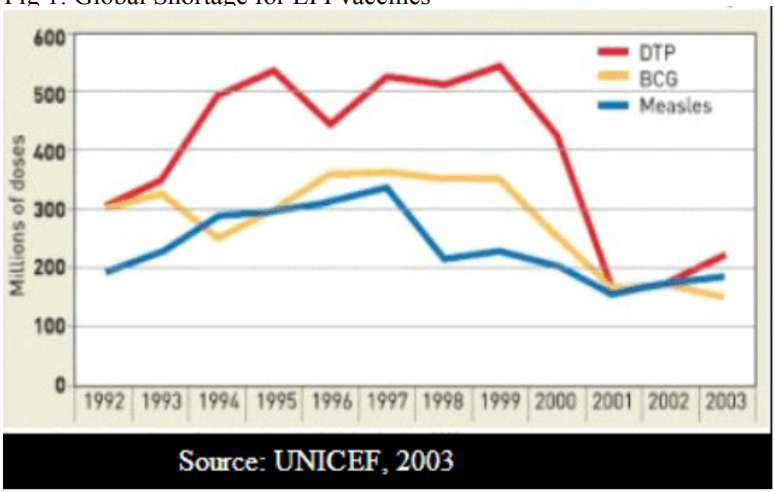
In January 2008, the Drug Controller General of India abruptly suspended production in the three vaccine public sector units (PSUs), the Central Research Institute (CRI, Kasauli, in Himachal Pradesh), Pasteur Institute of India (PII, Coonoor, Tamilnadu) and the BCG Vaccine Lab, (BCGVL, Chennai, Tamil Nadu) alleging that they do not comply with the current World Health Organisation's (WHO) Good Manufacturing Practices (cGMP). This put the national immunisation programme under crisis. Around this time, the Union Health Ministry announced the upcoming new vaccine park in Chengalpattu in Tamil Nadu based on public-private partnership model that was expected to meet the upcoming Universal Immunisation Programme (UIP) vaccine requirements by 2011 [Ramachandran 2008].

This raised several eyebrows and some pertinent questions such as 1) Why PSUs were not given a chance to upgrade to WHO-cGMP compliance, when they were under the very same union health ministry, especially at a time when their productions had peaked and the vaccine demand supply gaps were narrowing down, and there had been no complaints at all on the quality of the vaccines produced? 2) Why were PSUs asked to stop production even before the proposed centralised GMP compliant vaccine park

became operational at Chengalpattu, Tamil Nadu? 3) How would the Government meet the demand-supply gap of universal vaccines till the new vaccine park commences production, especially at a time when there is a short supply of primary vaccines the world over (http://www.unicef.org/supply/ index_vaccine_security.html>) (Fig.1) with very few primary vaccine manufacturers? What was the economic logic of spending over Rs.150 crore on building a new vaccine park when modernising existing PSUs would have cost less than Rs. 50 crore? Will the new companies that come up in the vaccine park really manufacture the vaccines indigenously or repackage them from the imported bulk?

If they import, what is the point in achieving GMP compliance at the cost of indigenous manufacturing ability? If dependence on private sector supply or import is inevitable, how will the government tackle concerns of biosecurity and strategic national health security? [Madhavi 2008]

Fig 1: Global Shortage for EPI vaccines



Though several Indian PSUs involved in vaccine production have been closed down in the last 15 years (Table1), and despite the role of the remaining PSUs in narrowing demand-supply gaps for universal vaccines by 2006 (Table 2), demand-supply gaps for universal vaccines peaked during 2008 (Table 3) with the closure of three vaccine public sector units that have major contribution to the country's UIP vaccine requirement (`70 per cent of DTP and 100 per cent BCG). Despite the private sector's promise of meeting UIP vaccines at par with the prices of PSUs, the shortages for UIP vaccines continue

till today [Ramachandran 2009]. In this context, this paper traces and analyses the trajectory of public and private sector's roles and access to stable and affordable supply of vaccines needed by the national immunisation programme, especially in the current context of changing socio-economic-political scenario, and implications for national vaccine policy.

Procurement of UIP vaccines

The Bhore Committee Report 1946 indicated that the child mortality due to infectious diseases was very high in India and it needed to improve child health status to improve the health of the nation [GOI 1946a]. Though there was house-to- house BCG vaccination programme after BCG vaccine laboratory was set up in 1948 in Chennai (then Madras), regular vaccination of children against infectious diseases in India was adopted only in 1978 in alignment with WHO's policy of "Health for all by 2000AD" that underlined primary health care approach. India adopted tetanus txoid (TT), diphtheria toxoid (DT), diphtheria, pertussis, tetanus toxid (DPT), oral polio vaccine (OPV), Bacillus Calmette Guerin (BCG) and Typhoid vaccines under its Expanded Programme on Immunization (EPI) to vaccinate children regularly under primary health care. These vaccines are provided by government in India free of cost in all primary health care centers. Since they were launched as EPI programme they are referred to as EPI vaccines. These vaccines are also called primary or universal vaccines as they are under the national immunization programme and vaccines against diseases such as Japanese Encephalitis, Cholera, Yellow fever, Hepatitis B etc., were classified as secondary vaccines as they are given as per the demand.

Subsequently, primary or EPI vaccines have come to be known as universal vaccines, with the launch of Universal Immunisation Programme (UIP) in 1985 aimed to achieve ~85 per cent immunization coverage in children and pregnant women by 1990. In 1985, measles vaccine was introduced under UIP and typhoid vaccine was excluded. The UIP was adopted as a Technology Mission launched by the Ministry of Health and Family Welfare with the Department of Biotechnology (DBT) as the nodal agency to support the UIP programme by promoting vaccine R&D towards self- reliance in vaccine technology and self-sufficiency in vaccine production (GOI 1987-88). This was the first time some policy aspects of vaccine development, production and immunization were articulated by the Union Government, though a clear, coherent and comprehensive national vaccine policy was never adopted. This is partly the reason why national vaccine production in general and PSUs n particular drifted away from the original objectives of self-reliance and self-sufficiency.

It was not difficult for India to meet the objectives of UIP with its fairly institutionalized

Table 1: Fate of Vaccine Public Sectors Units (PSUs) in India By 2008		
Vaccine PSU	Year of Establishment	Vaccines/Sera Produced
1. Haffkine Institute, Mumbai. (then Bombay Bacteriological Laboratory)	1898	DT, TT, Plague, Cholera, typhoid, rabies, gas gangerene anti-toxins, anti-dysentry, anti-snake venum
2. Pasteur Institute of India, Kasauli.	1900	Anti-rabies, (closed down)
3. King Institute of Preventive Medicine, Guindy, Chennai. (then Madras)	1898	Vaccine lymph, TT, Typhoid, cholera (production suspended in 2005)
4. *Central Research Institute, kasauli.	1905	Typhoid, cholera anti-snake venum, anti-rabies (production suspended in Jan 2008)
5. *Pasteur institute of Southern India, Coonoor.	1907	Anti-rabies, OPV (1967-1976), DTP, DT, TT (since 1978) (production suspended in Jan 2008)
6. *BCG vaccine lab, Guindy, Chennai.	1946	BCG vaccine (suspended production in Jan 2008)
7. The Pasteur & Medical Research Institute, Shillong, Assam.	1917	Typhoid, cholera, anti-rabies treatment (closed down in 2006)
8. Vaccine Lymph Department, Belgaum.	1904	Vaccine lymph (production stopped, closed down in 1980s)
9. Vaccine Lymph Department, Calcutta.	1890s	Vaccine lymph (closed down in 1980s)
10. The Cholera Vaccine Lab, Calcutta.	1890s	Cholera (closed down in 1980s)
11. Pasteur institute, Calcutta.	1910	Anti-rabies (not satisfactory functioning, now it is a teaching institute) (closed down in 1980s)
12. The Bengal public health Lab, Calcutta.	1900	Cholera, now conducts sterility tests of other govt. labs (since mid 1980s)
13. The Provincial Hygiene Institute, Lucknow.	1900	Cholera (closed down recently)
14. The vaccine Lymph Dept., Patwada Nagar (now called State vaccine Institute)	1903	Vaccine lymph, anti-rabies (closed down 2003)
15. The vaccine Institute, Ranchi.	1900	Vaccine lymph, cholera, anti-rabies (closed down recently)
16. The School of Tropical Medicine, Calcutta.	1921	Epidemiological and other routine diagnostic services. No vaccine production (since 1980s)
17. Institute of Preventive Medicine, Hyderabad. (Then Plague Department).	1870	Plague, Smallpox (since 1910), rabies (since 1976-77)TT (since 1978) (production of anti-rabies, TT stopped in 2002 and the company was closed down in 2005)

18. Vaccine Institute, Vadodara.. (became PSU in 1973)	1973	Anti-rabies (closed down recently)
19. Public Health Laboratory, Tiruvananth Puram.	1937	Anti-rabies, Now functions as immunology lab, supplies yellow fever vaccine on demand. (closed down)
20. Public Health Laboratory, Patna.	1900	Cholera (closed down recently)
21. Public Health Laboratory, Bangalore.	1900	cholera (closed down)
22. Indian Immunologicals Ltd., Hyderabad.	1983	Main focus on veterinary vaccines Human vaccine production began in the year: Tissue culture human rabies vaccine (1998) Measles, MMR(2002) RDNA HepB (2006) Rabies anti serum
23. Bharat Imunological and biologicals Ltd., (BIBCOL), Bulandshar Delhi.	1989	OPV formulations from imported bulk
24. Indian Vaccines corporation Ltd., (IVCOL), Gurgaon.	1989	Closed down in 1992
Bengal Immunity Ltd, Calcutta (became public sector in 1980s)	1919	All vaccines required for EPI, cholera, typhoid, anti-rabies, anti-snake venums etc., (closed down 2003)
25. Bengal Chemicals and Pharmaceuticals ltd., Kolkata. (established in 1901 as private company, became PSU in 1980)	1901	Chemicals, synthetics, Dyes and vaccines/sera (Closed down in 2000 and being revived recently)
26. Smithstrain Street Pharmaceuticals Ltd., (established in 1821 as private company, became PSU in 1977)	1821	Vaccines/sera (Closed down in 2000)
27. Vaccine Institute, Nagpur. (established in 1959 and became PSU in 1980)	1959	Smallpox, cholera (since 1968) production was stopped before it is closed down in post 2000
28. West Bengal lab Calcutta (became PSU in 1980)	1980	Produced sera/vaccines in addition to synthetics and dyes (Closed down in post 2000)

* suspended production in Jan 2008.
Source: Compiled from Annual reports of health and Family Welfare, Health Information of India, MOHFW, GOI, New Delhi.

vaccine R&D and production. Several institutions that were set up during British India were restructured to produce DTP group of vaccines since 1978. BCG vaccine was supplied by BCGVL for the entire country. However, 100 per cent of OPV and measles vaccine was imported to meet theI requirements of UIP. Measles vaccine was not produced in the country, as technology was not available. Since 1992, the entire measles vaccine required for UIP has been met by a private company, Serum Institute of India,

Table 2: Demand and Supply of UIP vaccines								
UIP vaccines	**1991-92 (lakh doses)**		**1995-96 (lakh doses)**		**2005- 06 (lakh doses)**		**2006-07 Upto March 07 (lakh doses)**	
	Demand	**Supply**	**Demand**	**Supply**	**Demand**	**Supply**	**Demand**	**Supply**
DPT	1320.24	1270.30	1362.20	182.50	2813.38	3226.90	1916.96	1636.88
DT	350.00	650.82	360.00	820.00	472.80	283.27	378.01	370.29
TT	1190.00	2319.71	140.00	529.00	6949.47	5410.60	3651.45	2887.94
BCG	500.60	168.50	550.00	350.00	637.0	637.0	894.94	758.66
OPV*	1550.60	*950.50	534.00	600.00	1698.96	1699.27	4823.66	4812.48
Measles	500.00	680.00	550.00	700.00	2240.23	2240.23	2688.10	2688.10
Source: Compiled from Annual Reports of Health Information of India 1991-92 and National Health Profile 2008, DGHS, India. *All imported Source								

Pune, that bought technology from elsewhere [Madhavi 1997]. Since 2002, Indian Immunologicals Ltd., Hyderabad (IIL), a PSU under National Dairy Development Board (NDDB) also started the manufacture of measles vaccine indigenously and supplies some amount to UIP. BCG supply from BCGVL became self-sufficient since 2002. OPV was also produced indigenously since late 1990s in HBPCL Mumbai that supplied OPV to UIP. Though, PII Coonoor produced polio vaccine indigenously between 1967-76, due to unexplained reasons, OPV production was stopped abruptly [Madhavi 2007]. Since then OPV has become a major import. Thus, DTP, TT, DT and BCG are produced indigenously in the country in the public funded organizations that largely took care of UPI requirements, though a few private companies (Bengal immunity ltd., Bengal Chemicals and Pharmaceuticals Ltd., etc.) also supplied small quantities to UIP. The country was able to meet the annual UIP requirements by importing some quantities of DTP group of vaccines whenever there was insufficient production and supply of UIP vaccines and the demand-supply gaps for UIP vaccines were met to a large extent by 2007..

In 2008, the dramatic suspension of the 3 major vaccine PSUs that catered to most of the UIPneeds created the paradoxical situation that still exists in India: while there exists a critical shortage of childhood vaccines, there is also an abundance of new expensive vaccines and their combinations in the market, being promoted heavily through media advertisements, industry campaigns, medical dealers, private practitioners, professional bodies and others. The lack of a national vaccine policy has facilitated the growth of the new vaccine Market, while the current crisis for universal vaccines peaked.

The success of a country's immunisation programme is determined by several local factors such as pathogen variations, incidence levels that qualify for mass vaccination, efficient

disease surveillance system, development and/or procurement of vaccines, choice of technologies, choice of selective vs. universal vaccination (even among childhood vaccines), logistics, cost-benefit analyses, and resource mobilization [Madhavi 2005]. While these factors are important and complimentary to each other, this article focuses on only the fate of Indian indigenous vaccine production capacities and its implications for access to stable and affordable supply of universal vaccines.

II
Indian Vaccine PSUs

It would unjust if India forgets its past glory in vaccine research and production for over 100 years, and how these oldest vaccine institutions stood up to meet national needs in testing times (the first and second world wars and during epidemics), despite overloaded service functions, inadequate manpower and poor patronage from the state. India's venture into modern medical research began with vaccine research that was fairly institutionalized during British colonial rule in India. For example, i) a plague vaccine was developed first in India at the Haffkine Institute Mumbai; ii) CRI Kasauli was the first laboratory in the world to produce anti-Rabies vaccine, it is the only one of its kind in the South East Asia region for yellow fever vaccine, and also a certifying authority for all the vaccines produced in the country; iii) PII was the first institute in India to clinically evaluate the anti-rabies serum-vaccine therapy in 1917 in the treatment of human beings---PII Coonoor developed tissue culture rabies vaccine indigenously, and also manufactured relatively cheaper DTP-HB indigenously just before its closure [Ramachandran 2008] ; iv) the King Institute of Preventive Medicine, Chennai developed smallpox vaccine indigenously, through minor innovations, improved yields of anti-cholera vaccine and TT vaccine; and v) BCGVL proudly claims that it is the first and the only Institute under the Ministry of Health & Family Welfare, that was awarded ISO 9002 by M/s Bureau Veritas Quality International (BVQI), London to get international accredition including WHO cGMP requirements in 1994, and BCGVL became self-sufficient in BCG vaccine required for the entire country since 2002 (http://mohfw.nic.in/dghs.htm). Many of these PSUs also undertook minorprocess/protocol innovations in vaccine development and production that improved yields and reduced costs of production. There were three private companies set up between 1890-1910 to produce synthetics, dyes and other pharmaceutical products, that have also produced vaccines and sera against infectious diseases [Kumar 1998]. However, it is the public funded vaccine institutions that mainly developed, produced and met all national vaccination needs.

R&D and production were traditionally under the same roof to facilitate coordination,

Table 3: The Demand-Supply Gap Following Vaccine Procurement from Private Suppliers 2008-09 (in Lakh doses)				
Supplier	**Vaccine**	**Total order placed**	**Total requirement**	**Difference**
B.E Ltd., Hyderabad	TT	1, 360.00	1,708.00	348.00
B.E Ltd., Hyderabad	DPT	800.00	1, 579.87	
SII, Pune		300.00		
IIL., Hyderabad		63.00		
Total		1, 163.00		416.87
B.E Ltd., Hyderabad	DT	375.00	432.66	57.66
Bharat Biotech Ltd., Hyderabad	OPV	1, 350.00	1, 581.86	
HBPCL, Mumbai pipeline)		180.50		
Total		1, 530.50		51.36
SII, Pune	Measles	360.00	391.20	
IIL., Hyderabad		90.00		
Total		450.00		58.80
Excess procurement				
SII, Pune	BCG	600.00	759.21	159.21
Source: 34th Standing Parliamentary Committee on Health and Family Welfare, Submitted to Rajya Sabha 2008..				

Table 4 : Declining Budgetary Allocations

Company	1987-88	1988-89	1989-90	1990-91	1991-92	1992-93	1994-95	1995-96	1996-97	1997-98	98-99	99-2000	2004-2005
BIBCOL	10												
(For both)	550												
(For both)	453												
(For both)	4.09	0.2	0.0	0.0	0.0	3.0	5.31	0.05	0.05	0.00			
IVCOL				0.91	0.0	0.0	0.0	0.0	1.5	0.0	0.00	0.00	0.00

Source: Compiled from DBT Annual reports. BIBCOL: Bharat Imunological and biologicals Ltd., IVCOL: Indian Vaccine Corporation Ltd.

technology transfer and commercialisation. A few centrally sponsored institutions such as Central Research Institute Kasauli, BCGVL Chennai, and others set up under the respective states during British India to develop vaccines and sera against dog bites, snake bites, insect bites and infectious diseases that were a major public health threat at that time got restructured and reoriented to produce EPI vaccines since the launch of EPI in 1978. For instance, institutions such as PII Coonoor, CRI Kasauli, Institute of Preventive Medicine (IPM), Hyderabad etc., that were initially set up to develop vaccines and sera against rabies, also started production of DTP group of vaccines. With the declaration 88 Meeting Local Needs in Global Times: The Case of Universal Vaccines in India / Madhavi of India smallpox free in 1976, institutions such as KIPM, Chennai, Vaccine Institute Belgaum, Pasteur Institute Shillong etc., stopped smallpox

vaccine production and started the manufacture of TT, DT and DTP. At that time Hathi committee felt that the existing conventional technologies for the production of TT, DT and DTP were fine and recommended use of same techniques of production [GOI 1975]. These aged institutions continue to carry out multiple tasks including epidemiological investigations, water testing, production of reagents, diagnostic services, blood bank services, training of S&T staff, vaccine research, development, production and supply of vaccines even today, though the Hathi committee felt that the production and R&D functions should be separated and regional cenrtres should be established to carry out supply functions [GOI 1975].

Another significant development during mid 1970s was the government take over of private companies such as Bengal Chemicals and Pharmaceutical (BCPL) (1980), Bengal Immunity Limited, (BIL) (1977), Smith Strainstreet Pharmaceuticals Ltd., (SSPL) (1977), West Bengal Lab (1980) based in Calcutta (now Kolkata), Vaccine Institute Baroda (1973), and Vaccine Institute Nagpur (1980). Thus, the public sector units that produced primary vaccines increased in number by 1980s [Madhavi 2007]. Ironically, it is these very units that were closed down in post 1990s owing to liberalization in India

Though, DBT was formally established in 1986, it was functioning as board since 1982 to harness biotechnology for mankind and vaccines are one of main focus areas of the health under biotechnology. In the late 1980s the launch of UIP under Technology Mission gave a further boost to indigenous vaccine R&D and production and DBT was entrusted with the i) production of newer vaccines for UIP, and ii) to promote R&D for new and improved vaccines. DBT set up three expert/technical committees in 1988 evaluated the state-of-the-art technologies for the production of oral polio vaccine (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 and for the production of the measles vaccine the chick embryo fibroblast cell culture, and for OPV primary monkey kidney cell culture based technology [GoI various years]. Thus, DBT took the initiative to meet the demand-supply gaps for universal vaccines [GoI 1987-88].

In 1989 DBT setup two public sector units, Bharat Immunologicals and Biologicals Ltd. (BIBCOL), Bulandhshar and Indian Vaccine Corporation Ltd. (IVCOL), Gurgaon) to meet demand-supply gaps for universal vaccines. IVCOL was to produce 20 million doses of measles vaccine, 50 million doses of IPV and 40 million doses of DPTP. IVCOL was closed down in 1992 as technology for the production of measles was

Table 5: Reported Shortages of EPI Vaccines from Different States between Jan-Oct 2008	
State	Vaccine shortage
1. Haryana	TT for pregnant women (TT Pw), DPT
2. Andhra Pradesh	
3. Arunachal Pradesh	BCG
4. Andaman and Nicobar Islands	BCG
5. Assam	DPT, Measles
6. Bihar	DPT, BCG, Measles
7. Chandigarh	TT Pw, DPT, BCG
8. Chhattisgarh	DPT
9. Delhi	TT Pw, DPT, yellow fever (No DPT vial stock since mid July 08. No stock of yellow fever vaccine for last 4 months)
10. Gujarat	TT Pw, DPT
11. Himachal Pradesh	DPT
12. Jharkhand	TT Pw
13. Karnataka	TT Pw
14. Kerala	DPT, yellow fever (State requires eight lakh doses of vaccines a year against the 2.5 lakh doses provided by the Centre this year. The State cannot procure these vaccines locally as the Centre was not ready to fund their purchase)
15. Lakshwadeep	TT Pw, BCG
16. Madhya Pradesh	TT Pw
17. Maharastra	TT Pw, DPT yellow fever
18. Orissa	TT Pw and shortages of DPT, BCG, OPV and measles was also reported from Koraput district
19. Punjab	DPT
20. Rajasthan	TT Pw
21. Tamil Nadu	TT Pw, yellow fever
22. Uttar Pradesh	TT Pw
23. West Bengal	TT Pw, DPT
Source: Compiled from Newspapers and National Rural Health Mission (NRHM) Dec 2008.	

not available from Pasteur Merieux Serum & Vaccines (PMSV), France, as it became private company and India was viewed as potential future market for measles vaccine (Madhavi 1997). BIBCOL that was WHO-GMP certified, aimed to produce OPV and plasma derived Hepatitis B indigenously by 1992. However, BIBCOL was declared sick and IDBI was appointed to prepare a revival package in 2000 [Madhavi 2007]. The declining budgetary allocations to both the PSUs (Table 4) imply that it is not mere coincidence that both the PSUs set up by DBT failed during post liberalization

Table 6: Demand and Supply

Vaccine	2006-07			Private Sector supply in 2008-09		
	Demand	Supply	Shortage	Demand	Supply	Shortage
DPT	1916.96	1636.88	280.08	1579.87	1163.00	416.87
DT	378.01	370.29	7.72	432.66	375.00	57.66
TT	3651.45	2887.94	763.51	1708.00	1360.00	348.00
BCG	894.94	758.66	136.28	759.21	600.00	159.21
Measles	2688.10	2688.10	0.0	391.20	450.00	-58.81
OPV	4823.66	4812.18	11.48	1581.86	1530.50	51.36

period, thus drifting away from policy objectives and demand-supply gaps for universal vaccines continues to remain despite good intentions of the government.

The closure of PSUs in the last 15 years (See Table 1 and Fig. 2) has drastically affected the access to universal vaccines 30 years after the launching of EPI in 1978. As there was no demand for smallpox and cholera vaccines, five vaccine PSUs were closed down in 1980s. Around 14 Indian Vaccine PSUs were closed down during 2000-2008. Vaccine Institute Baroda, IPM Hyderabad, SVI Patwadanagar, Bengal Immunity, Kolkata, SVI Belgaum, BCPL Kolkata were closed down between 1995-2005, and PI Shillong was closed in 2006. In 2008, production was suspended in three PSUs (CRI, PII, BCGVL) and their conversion to testing labs was envisaged. However, the closure of PSUs in post 1990s seems to be slow withdrawal of state funding/support from these institutions due to the introduction economic liberalisation policies in India. By 2008 India was left with only three PSUs functioning one under Maharashtra state government (HBPCL, Mumbai), one under National Dairy Development Board (NDDB) and one under DBT (BIBCOL, Bulandshar). Though erratic production patterns (Fig. 3) and demand supply gaps for EPI vaccines were observed over the years (Table 2), demand-supply gaps for universal vaccines have peaked (Table 3) last year due to the suspension of production in three vaccine PSUs that made a major contribution of UIP vaccines, resulting into acute shortage in 23 states in India (Table 5 and 6).

Though, there have been national efforts since the launching of EPI in 1978, the changing roles of public sector and private sector in meeting vaccine requirements have precipitated last year's crisis of acute short supply of primary vaccines in India. A glance at current vaccine scenario in India indicate that despite fair vaccine production system in the country, production patterns of universal vaccines has always been erratic (Fig. 3) and demand supply gaps (Table 2) increased for all UIP vaccines despite national efforts through DBT [Madhavi 1997, 2007]. Over the years, declining role of public sector (Fig 2) and increasing role of private sector (Fig. 2) during post 1990s leading to the

declined production of UIP vaccines (Fig. 4) and increased production of new vaccines (Fig. 5).

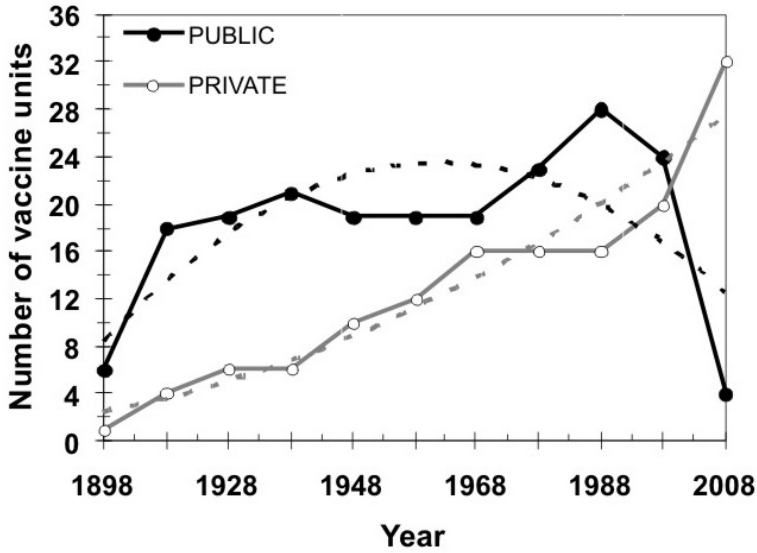
However, increased growth of private sector did not contribute to the increased production of UIP vaccines, due to private sector's low interest in UIP vaccines (Fig. 4) and its high interest in new vaccines (Fig. 5) leading to the orphanization of UIP vaccines in post 1990s in India. Further, demand supply gaps for universal vaccines peaked (Table 3) during the last year (January 2008) due to the suspension of production in three vaccine PSUs that account for 70 per cent of DTP and 100 per cent BCG of county's UIP requirement. This led to the severe shortages for UIP vaccines from 23 states within six months (Table 5). In some states even in urban areas some children did not receive 2nd and 3rd doses of vaccines due to their non-availability. It was reported that many states have run out of their supplies and the government has not allowed them to pick up even the existing stocks from the PSUs. Around 300 deaths were reported in a hospital in a remote village in Bihar out of 700 patients admitted suffering from diphetheria, tetanus and pertussis. According to the health ministry's data, compared to 2007-08, DPT vaccination in 2008-2009 (from April to November) fell by 29.5 per cent in Orissa and 36.2 per cent in West Bengal. BCG vaccination fell 7.9 per cent in Uttar Pradesh and 11.5 per cent in Punjab [Varshney 2009]. In fact, how India will resolve the current crisis of short supply of UIP vaccines, especially in the context of a global shortage for primary vaccines resulting from the decline of primary vaccine production in many companies, is a moot question and has implications for access to vaccines in future.

Changing production profiles of PSUs

Experienced vaccine PSUs not only did multiple tasks, but also changed production profiles as and when required, even till recently. For instance, during the first and second world wars they were forced by import restrictions to become self-reliant and self-sufficient in vaccine production [GoI 1946b]. In 1957 during influenza epidemics, PII, Coonoor carried out research to isolate and culture influenza virus to make the vaccine [Pasteur Institute 1957]. In 1976 after the country was declared smallpox free, KIPM Chennai adapted itself to produce DTP group of vaccines [KIPM 1985]. Similarly PII Coonoor produced OPV between 1967-76 indigenously and DTP group vaccines since 1978 till recently as per government orders. In 2006, PII Coonoor that was set up initially as a philanthropic organization to develop a vaccine against rabies and treat patients with dog bites was asked to stop its production after more than 100 yrs of its service. PII has been doing service to the nation through innovative treatment methods against dog bites, and was also producing a tissue culture based human anti-rabies vaccine indigenously since late 1997. Union health ministry orded PII to start the production of measles vaccine [Madhavi 2008].

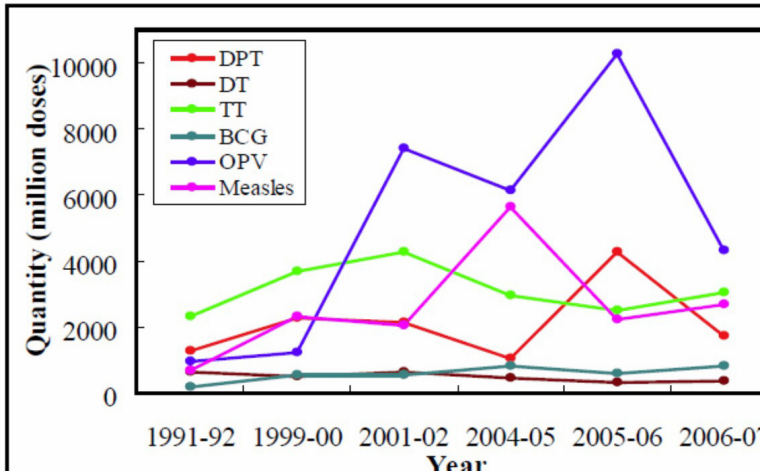
PII did oblige the ministry's request and bought measles vaccine from a newly set up private company Green Signal Bio Pharma based in Tamilnadu by the then PII director,

Fig 2: Growth dynamics of PSUs and private vaccine firms



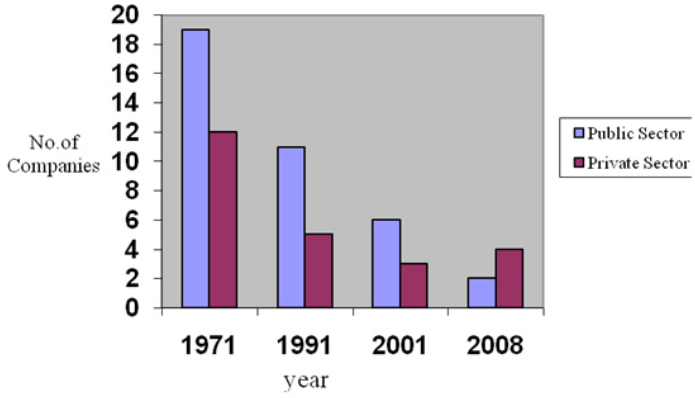
Source: Compiled from Annual Reports of Health information of India and National Health Profile 2008, DGHS, India.

Fig 3: Erratic production of UIP vaccines



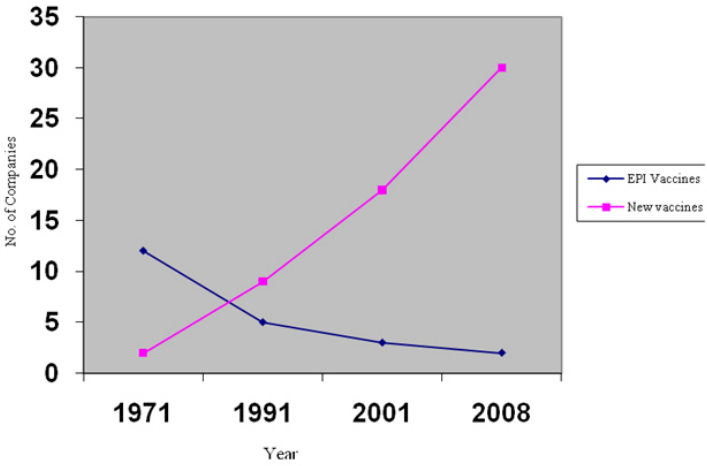
for Rs.3.25 crore, which was otherwise available virtually for free from another PSU, Indian Immunologicals Institute, Hyderabad. Interestingly, the Health Ministry sanctioned PII Rs 17.80 crore for branching out into measles vaccine production only after it entered into the deal with Green Signal Bio Pharma. According to media repots, the entire deal was allegedly executed to help the private company, as it stipulates that the PSU would produce measles vaccines from the seed and give away 70 per cent of the profit to Green Signal Bio Pharma [Gopikrishnan, 21st May 2008]. Objections have been raised in an audit on the misuse of financial powers and bypassing of procedures that were overlooked by the top functionaries of the ministry. Interestingly, Green Signal Bio Pharma could purchase BCG seed from the PSU, BCGVL (also headed at that time by the then PII director), for a mere Rs. 1.05 lakh, indicating that private firms get PSU resources for a song, whereas PSUs buy even free resources from favourite private firms by paying them the moon [Madhavi 2008]. One wonders, why PII was asked to change its production profile from anti-rabies to measles vaccine, when there was enough supply of measles vaccine from SII, Pune for UIP. It appears on the face of it that the indigenous manufacture of measlesvaccine is being encouraged/shifted to PSU by the union health ministry. However, on the contrary, media reports indicate that this is only to favour two new private vaccine companies based in Chennai. While the reasons for changing production profiles in PSUsmay be political, PSUs always obliged the parent ministry's orders and were willing to adopt to the changes as and when required despite difficulties.

Fig 4: Primary vaccine Suppliers to Indian EPI in The Last Four Decades



Source: Compiled from Annual Reports of Health information of India 1991-92 to 2004-05 and National Health Profile 2008, Directorate General of Health Services (DGHS), India.

Fig. 5: The Growth of Private Sector in Indian Vaccine Market



Source: Compiled from annual reports of Health information of India and National Health Profife, DGHS, India

These instances illustrates that unfortunately that PSU resources (raw material, skilled manpower, know-how, etc.) were often utilized to the full in such a manner that the PSUs benefited the least and the private sector the most. To cite few more examples, the famous private vaccine company Serum Institute of India, based in Pune was formed with erstwhile employees of Haffkine institute in 1960s. Even the newly set up Shantha Biotech in late 1990s derived inputs for Hepatitis B indigenous production from public funded organizations for developing technology, skilled manpower as well as infrastructure and institutional support [Hari 1997]. Moreover, Shantha Biotechnics which developed an indigenous hepatitis-B vaccine and was the most pampered by Indian government as a model for home-grown, government-supported private enterprise, has now been taken over by the French multinational company (MNC), Institut Merieux and is being eyed up by another MNC GlaxoSmithKline. This situation not only increased the uncertainty in availing affordable vaccines, but also affected public sector scientists who transferred technologies, as Shantha no longer honours its commitments to them. Hindustan Health Care Limited (earlier Hindustan Latex Ltd.) a PSU given charge of upcoming vaccine park (under public private partnerships) is also planning to access technologies from the existing PSUs for primary vaccine production in vaccine park, while new vaccine production is envisaged through public private partnerships.

It is not an exaggeration to state that today Indian private sector's indigenous capacity would not have existed if there is no indigenous public sector. Thus, promoting private sector at the cost of PSUs amounts to killing indigenous vaccine capacities/strengths,

especially at a time when developed countries like US, UK are reconsidering to revive their PSUs in view of biosecurity/national security [Bunn 2008; Blume and Geesink 2000]. In some European countries like Netherlands, vaccine PSUs have traditionally been serving the national vaccine needs and continue to do so today. The Netherlands Vaccine Institute (RVI) is an agency of the Dutch Ministry of Health, whose core task is to guarantee the supply of vaccines for national immunisation programmes, by in-house production or by manufacturing vaccines under license from pharmaceutical companies. A US Institute of Medicine report on vaccine development recommended a government-owned vaccine research and production facility to produce vaccines against emerging disease threats and bioterrorism. In United States, shortages of several paediatric vaccines occurred between 2000-2002 due to the private manufacturers changing production profiles from UIP (eg.TT) vaccines to new vaccines (pneumococcal vaccine). This left only one other national producer, which did not have enough time to meet the shortfall. In 2004, the MHRA suspended Chiron's manufacturing license for its influenza plant in Liverpool due to contamination. The company was scheduled to supply approximately 48 million doses to the US; it did not produce vaccine for a year whilst addressing the problems [Anon]. Seasonal influenza vaccine manufacturing problems affecting the UK''s supply occurred in 2005 and 2006. However, this did not affect the number of doses reaching patients since more than one manufacturer contracted by the Department of Health was producing the vaccine. This illustrates how reliance on a single supplier can leave the national health systems exposed, a concern raised by the House of Commons Public Accounts Select Committee in 2003 [PAC 2004]. It is evident that even in developed countries UIP has been affected because of its reliance on single and private manufacturer.

Indian PSUs have done dependable services to the national immunization needs by developing, manufacturing and supplying UIP vaccines, besides carrying out a range of other public health services. Yet, they did not receive enough patronage from the ministries under which they were functioning, despite their inherent interest. The case of Haffkine Institute is a reflection of state of affairs in many older vaccine institutions [Madhavi 2000].

The government support received by these public sector units was for only enhancing production capacities, and they did not receive much deserved support for upgrading infrastructure, R&D, technological growth and compliance to good manufacturing practices (GMP). Moreover, there were no changes in their governing bodies since their inception and lack of vision on their part to promote R&D through incentives that can be inbuilt with in the institutional structures, neglect, and bureaucratic controls added

to the systematic decline of the state patronage of PSUs. Even the policies of economic liberalization in 1990s did not enhance the functional autonomy of the vaccine PSUs. It is ironic that no money was sanctioned for their cGMP upgradation worth (Rs 50 crore), while generous sanction was given to the tune of Rs 150 crore on the upcoming vaccine park. On the contrary, supporting and reviving PSUs became politically unfashionable and blaming the PSUs and manufacturing political consent for their closure became the favourite pastime of the powers that be. Operationally, starving and stifling PSUs till they failed to meet some regulatory requirements was a safe strategy, as the action taken on the PSUs would seem like an act of good governance [Madhavi 2008]. Thus, the attenuation of PSUs has severely affected the indigenous manufacturing capability, and has also led to the orphanization of primary vaccines. While some of the remaining vaccine PSUs have already become importers and repackaging units over the years, skeptics fear that the Hindustan Healthcare Ltd., though a PSU (does not have the technology, experience or credibility to manufacture world-class vaccines as compared to any of the Indian vaccine PSUs) likely to go down the same path of bottling and repackaging of imported stocks or enter into the public-private partnerships [Ramachandran 2008].

The fate of PSUs in this country and their credibility in meeting national vaccine needs and with private sector's uncertain behaviour indicate that the private sector at best can be complementary to public sector with good governance in place, but it cannot be a replacement in view of national public health and bio security concerns. How the government is going to meet the current crisis of short supply of UIP vaccines, with private sector going back on its promise and vaccine park coming up only in 2011 is bigger challenge to face.

III
Private Sector in Vaccines

Indian vaccine private sector began to grow in late 1980s. Today there are around 30 companies (Table 7, Fig. 2) manufacturing and marketing vaccines in contrast to three functional PSUs in the country. One would have expected that the growth of private sector would meet the void (for universal vaccines) created by public sector's closure. That has not been the case. The private companies policy of prioritizing their new

Table 7: Private Vaccine Business in India

Vaccine Institute	Year of establishment	Vaccines/sera produced
1. Serum Institute of India, Pune	1966	TT(1972), DTP, tetanus anti-toxin, measles vaccine(1989), Rubella (1992) MR& MMR (1993), DTP-IPV(1985), r-HB(2001), BCG(2002), HDC rabies (2004), DTP-HB(2005), Hib (2007)

2.Shantah Biotech, hyderabad	1993	r-Hb, DTP-HB (2005) and JE vaccine
3. Panacea Biotech, Delhi	1984	OPV, r-Hb, DTP-HB, DTP-Hib, DTP-HB-Hib
4. Biological Evans Ltd., Hyderabad	1953	DTP, TT, R-HB (2004)
5. Cadila laboratories	1952	Typhoid
6. Bharat Biotech International Ltd., Hyderabad	1996	R-HB (without cesium chloride), typhoid, anti-rabies (2006)
7. Zydus Cadila (a divison zydus biogene manufactures vaccines)	1995	R-HB, typhoid, anti-rabies chicken pox vac
8. Biovaccines Pvt. Ltd., Hyderabad	1977	TT
9. LG lifesciences India Pvt. Ltd.,	2002	r-HB
10. Unichem Laboratories Ltd., Mumbai	1944 but ventured into biotech business in 2001 including vaccines	r-HB
11. VHB Life sciences Inc	1946 and marketed OPV in 1960-70 and new vaccines since 1984 (Hb vaccines to others)	R-HB, typhoid, anti-rabies, varicella vaccine
12.Solvay Pharma India Ltd., Mumbai	Since 2004	Markets Netherland's Influenza vaccine
13.Intas Biopharmaceuticals Ltd., Ahmadabd	2000	r-HB
14. Pfizer India Ltd.	mid 1990s	Markets r-HB made in USA and also shantha biotechs Hb vac
15. Wyeth India Ltd., Mumbai	Started as ledrle lab ltd in 1947 and later changed its name to cynamid Uindia ltd and in 1962 and became Public sector. In 1998 3 copanies merged as Wyeth Ledrle lTd and in 2003 as Wyeth Ltd., a MNC company now.	Markets Hib, DTP, prevenar since late 1990s
16. Chowgule & Co. (India)	Late 1940s	Triple antigen
17. GlaxoSmithKline India	Established in 1924 used to produce vaccines and in 1970s it business is more on other medicines and in post 1990s ventured into new vaccines	Varicella, DTP-HB, Hb, Hib conjugate, DPT, Hepatitis A, Hb-TT
18. Sanofi Pasteur India Ltd.,	1997	Typhoid, Hib, anti-rabies, varicella, OPV, combination vacs, Pneumococcal, Hb, Hepatitis A, meningococcal
19.Zydus Cadila Healthcare Ltd., Ahmadabad	2002	Varicella, typhoid,

20. Chiron Behring vaccines Ltd., Ankelswar India	In 1978, and Hoecst sold its rabies manufacturing unit to Chiron Behring vaccines India ltd., and taken over by Aventis and now by Sanofi pasteur	Markets all new vaccines
21. Bharat Serums and vaccines Private ltd.,	1971	In1970s produced DPT group vaccines and in 1990 markets vaccines like typhoid etc.
22. Biomedical Private Ltd., Ghaziabad	2000	OPV, typhoid
23. Dano vaccine & Bio hyderabad,	2000	TT
24. Prime vaccine Pvt. Ltd., Hyderabad	2000	TT
25. Transgene biotech Ltd., Hyderabad	2000	typhoid
26. B M pharmaceuticals Bhuveneswar	1999	Suppliers of Anti-snake and anti-rabies liquid and freeze dried vacs
27. Childcare Biotech Ltd., jalgaon, Maharashtra	2000	TT pertussis other vaccines
28. Ruchi Networks, New Delhi	Post 2000	Vaccine makers & suppliers Anti-cancer vacs
29.Ishitha Phrama Mumbai	Post 2000	Vaccine makers & suppliers: Entire range of human vaccines like Polio, DTP, DTAP, Dual, Measles, MMR, Hepatitis A, Hepatitis B, BCG, Chicken Pox, Anti rabies, etc. Anti : HIV Vaccine Hepatitis A and combination vaccines
30. Rajgarhia Drug Agencies, Ranchi	1982	Vaccine distributors
31. Wockhadt mumbai	1959	Markets vaccines in post 2000
Source: Compiled from websites and annual reports of companies http://pharmaceuticals.indiabizclub.com/directory/vaccines; http://mohfw.nic.in/dofw%20website/family%20welfare%20programme/vaccines.ht and (http//www.nature.com/nbt/journal/v25/n4/fig_tab/nbt0407-403_T4.html		

HiB: influenza type b, TB: Tuberculosis, DPT: Diphtheria Pertusis Tetanus, HB: Hepatitis B, IBR: infectious bovine rhinotracheitis, HPV: human papillomavirus, BCG: Bacille Calmette-Guérin, OPV: Oral polio vaccine, DT: Diphtheria tetanus, MMR: Measles, mumps, and rubella, DTaP: Diphtheria tetanus Pertusis, TT: Tetanus toxide, AP: Alum Precipitated, BQ: Black Quarter, C-19: Cotton Strain-19, FD: Freeze Dried, GTV: Goat-adapted Tissue vaccine, HS: Haemorrhagic Septicaemia, OA: Oil Adjuvant, RP: Rinderpest and TCV: Tissue Culture Vaccine.

Vaccine business (Fig 5) over UIP vaccines (Fig 4) has only aggravated the situation. Though private sector set up DTP production plants, they are more interested in making new non-UIP vaccines or their dubious value-added combinations, rather than supplying the DTP for the government's UIP. While it may be true that the overall production in

the last couple of years (till the public sector units were closed) has increased to meet the demand, this growth in production may have come from two sources. 1) The PSU's themselves pushed up their production in the last few years, perhaps in a last ditch attempt to prevent their imminent closure- which itself may have diverted their attention from GMP. 2) The private sector seems to have recently enhanced its production of UIP vaccines (strangely enough, considering their earlier disinterest despite mounting shortages), in anticipation of the closure of the PSUs.

It is evident from last year's (2008) experience that the shortages of UIP vaccines in 2008-09 are much more when compared to previous years (Table 6), even with few sinking PSUs by 2006 and despite private sector's promise to the union health ministry that it would supply to Indian UIP at par with PSU prices. On the other hand the private sector units that promised to supply UIP for one year at subsidized prices started complaining by July 2008 that their revenue has gone down by 22 per cent due to this supply and they may not be able to supply UIP vaccines at the same price in the following year (Biospectrum 2008). The situation has not improved even after one year. In fact, the health ministry was forced to get vaccines illegally from the very public sector manufacturers it suspended previous year (2008). In 2008-2009, the government has bought DPT worth Rs 1.1 crore; DT worth Rs 30 lakh and Rs 1.2 crore worth of TT from the Central Research Institute, Kasauli [Varshney 2009]. This indicates that it is the public sector that is responding to UIP needs in the midst of its own crisis for survival. According to some officials in the procurement wing of health ministry, private manufacturers had hiked prices and not supported the nation during a crisis. The vaccine cost for diphtheria, pertussis, tetanus and BCG for 2008-09 turned out to be Rs 64.29 crore, compared to Rs 32.20 crore the previous year. It was also not clear from table 3, why ministry has placed order for more quantity of measles vaccine than required [Varshney 2009].

Clearly, it makes economic sense to depend on the public sector for the supply of affordable vaccines for the universal immunization programme, rather than leaving the health security of the country to the mercy of the private industries and politicians. These instances prove that the private sector in no way matches public sector's willingness and promptness in meeting national needs unless they are made to do so. Only good governance with good regulatory system in place can ensure access to vaccines through private sector.

Regulations ensuring access to universal vaccines

Vaccine production was stopped abruptly in three existing PSUs (CRI, Kasauli, PII, Coonoor, and BCGVL, Chennai, TN), in Jan 2008, by Drug Controller General of

India (DCGI) alleging that they were not compliant with current "Good Manufacturing Practices" (cGMP). It was pointed out by the health ministry that they had no option but to close these units as WHO would derecognise the Indian National Regulatory Authority (NRA), if Indian companies do not meet WHO-cGMP standards. WHO-GMP is a certification of a process adopted by the World Health Organisation to ensure that products are consistently produced and controlled according to quality standards. It's objective was to set up uniform global standards to minimize the risks (contamination, causing damage incorrect labels on containers, insufficient or too much active ingredient, ineffective treatment or adverse effects, etc.) involved in any pharmaceutical production that cannot be eliminated through testing the final product. Many countries have formulated their own requirements for GMP based on WHO-GMP. India's Schedule M is comparable to WHO-GMP, that is awarded and certified on behalf of WHO by the DCGI under ministry of health and family welfare (MOHFW).

Though, these PSUs could meet GMP standards earlier in 2001 and 2004, they could not meet them in 2007 as they were made more stringent, referred to as current GMP standards (cGMP), and companies have to become cGMP complaint every time with the latest modifications in WHO-GMP guidelines. The stringent rules in the current GMP standards are related to structural, process and documentation deficiencies, and the institutes could rectify process deficiencies but could not rectify structural and documentation deficiencies [Ramachandran 2008]. The institutes stated in their reply to the DCGI that limited funds and lack of functional autonomy in recruitments, promotions, maintaining staff, finances, structure etc., and the lack of flexibility in running these biological industrial units due to bureaucratic limitations as the reasons for their inability to comply with the GMP norms [Madhavi 2008]. While it is desirable that PSUs should become cGMP complaint, government's action of closure in haste without making reliable alternative arrangements (till vaccine park comes up) to meet resultant short supplies of UIP vaccines met severe criticism. The government had the following options to exercise, yet, it did not, that led to skepticism.

1. Since the expenditure of making PSUs WHO-cGMP compliant is meager compared to costs on upcoming vaccine Park, the health ministry should have sanctioned the money by giving a chance to PSUs. Critics wondered why the ministry, that owns and governs the vaccine PSUs, could not wait till they were made compliant with the increasingly stringent GMP norms, before taking such a drastic action on them, despite PSUs request to sanction money in order to become GMP-compliant.

Moreover, the health ministry did not accept the WHO offer to help them to become cGMP compliant[Rajya Sabha Secretariat 2009]. It is not a big deal to make these PSUs GMP complaint as many of Indian pharmaceutical companies including Indian private

vaccine companies such as serum institute of India, Shantha biotech, Panacea biotech, have WHO-GMP certification and have complied with much tougher requirements of US FDA and EU and WHO's pre qualification requirements for export. About 800 Indian drug companies including big, medium, and small are WHO-GMP complaint for making a wide range of liquids, tablets, capsules, injections, bulk drugs and vaccines and sera. And about 40 Indian drug companies (very few of them MNCs) have been approved by international regulatory agencies of UK, USA, Australia, EU, Brazil, etc. (www.pharmabiz.com). Spending a few crores of Rupees on vaccine PSUs is meager when compared to the money spent on vaccine park that would come up only after 3 years, and also when compared to the costs of purchasing imported vaccines from private companies. Most importantly, costs on child health due to non-availability of universal vaccines and the possibility of rise of childhood diseases and treatment costs would be of grave national public health concern.

2. PSUs should have been allowed to produce UIP vaccines till they become cGMP compliant, as there is no complaint about the quality of vaccines produced by these PSUs. It is not clear whether stringent application of GMP norms were applicable only to vaccine PSUs or to the Pharmaceutical industry as a whole, since there seem to be many private Pharmaceutical companies that operate without GMP certification. The 34th Parliamentary Committee pointed out that the GMP status of private company Biological Evans that supplies vaccines to UIP is not very clear. The ministry did not hesitate to import Japanese Encephalitis vaccine in 2006 from GMP noncompliant Chinese manufacturers. The ministry is also aware that Chinese exports were neither hit due to their non-compliance, nor was the Chinese NRA de-recognized by the WHO [Ramachandran 2006]. Clearly, the Chinese Government seem to handle the WHO and its NRA better than the Indian Government [Ramachandran 2008].

3. Since cGMP is required for exports through WHO-UNICEF, the DCGI had the option of banning PSUs from exports until they were made cGMP complaint and till the vaccine park come up. Critiques pointed out that if Indian NRA is derecognised by WHO it would hit private vaccine units rather than PSUs. According to former health minister Ramadoss, "Derecognising Indian NRA as a country means even private units that are CGMP certified will not be able to export. Today India exports vaccines worth nearly Rs.1,000 crore to international agencies, such as UNICEF, all of which will be cancelled." It appears that the ministry was more interested in private sectors exports, than the consequences of sudden closure with the resultant severe short supply of UIP vaccines. Compliance with WHO-GMP is mandatory only for exporting vaccines or buying them through the UNICEF vaccine procurement system and not for indigenous

manufacture/purchase/immunization. That means that the DCGI and the health ministry had the option of suspending only exports till the PSUs became GMP compliant to meet indigenous demand, considering the fact that there was no complaint on the quality of the vaccines produced in those PSUs. Vaccine Institute (RIV) under the Dutch ministry in Netherlands improved Salk's injectable polio vaccine (IPV) vaccine, and the incentive came both from the country's commitment to a particular immunisation schedule (the combined polio and DPT vaccine) and from technical achievements that reduced dependence on wild monkeys, and this vaccine has been insulated from market forces as the Dutch ministry was not interested in exports [Blume and Geesink 2000]. Indeed China, Netherlands and other countries have effectively exercised this option to protect their PSUs and indigenous public health needs from the vagaries of international regulation. India is making quality medicines and vaccines for years without a WHO-GMP and by following their own idea of aseptic clean manufacture, and without any reported fatalities, it is argued that that the setting up uniform global standards such as good manufacturing practices (GMP), good lab practices (GLP), global intellectual property regimes (IPR) tend to become trade barriers in the form of International Conference on Harmonization (ICH), to inhibit countries like India from entering the international trade (personal communication, Srinivasan, LoCost). Before the last Genereal Elections, there were rumours in the media that these three PSUs were going to be reopened due to public furore.

However, other reports [Nagarajan 2008] pointed out that the ministry may simply be buying time till the upcoming elections of May 2009. Even though the PSUs would be revived, they would not be asked to produce anti-rabies, DTP and BCG, but other vaccines. That means by not allowing Vaccine PSUs to produce vaccines in which their expertise lies, that comprises 80 per cent of the Indian UIP market, the PSUs would be rendered redundant. On the other hand, since the closure of CRI affected private companies' vaccine exports, (worth 1,500 crore) as CRI Kasauli certifies all vaccines before release for consumption, It is predicted that the government might reopen these units, though the threat to convert these institutes to testing labs still remains. In September 2008, WHO did not approve any new vaccine from India temporarily as Indian NRA failed its quality bench marks [Mathew 2008]. Companies like Shantha Biotech, Panacea Biotech and Serum Institute of India are eagerly waiting to supply new vaccines to WHO-UNICEF procurement system, while they refused to meet national UIP vaccine shortages. The same private companies, beneficiaries of PSUs closure, that were very critical about PSUs GMP standards, also justified their closure. However, the same private vaccine companies were very eager by September 2008 that these PSUs should be revived, since derecognition of Indian NRA by WHO would be a deathblow

to private sector vaccine business. According to the consultancy firm KPMG, vaccines dominate the Indian biopharma market and contribute about 51 per cent of its $1.4 billion revenues. [Varshney 2009].

4. The health ministry could have exercised the choice of making the private sector supply to UIP vaccines at affordable prices with appropriate regulations till the PSUs become GMP compliant and till the Vaccine Park is ready. Indian experience reveals that private sector is not a reliable option for stable and affordable supply of vaccines. Doubts have been expressed regarding the upcoming Vaccine Park, and whether the public sector unit, Hindustan Healthcare Limited (HHL) (then HLL) that does not have any expertise in vaccines whatsoever (except that it mediated occasional import of some vaccines to the government), would be able to manufacture quality vaccines and remain WHO-cGMP compliant forever in the upcoming park. Moreover, there is no guarantee that HHL would not meet the same fate as these three public sector units in the near future. Also, whether the public private partnerships (PPP) in the Vaccine Park are going to be cGMP complaint and produce quality vaccines or are they going to supply imported vaccines is anybody's guess. Most, importantly, how is the Indian government prepared to deal with any similar crisis that may arise in future? Given that the plan for vaccine park and future vaccine market in India was projected by Earnst & Young, a US based consultancy organization, many wonder whether this vaccine park through PPPs is not surreptitiously meant for multinational corporations to produce or supply new vaccines.

It is not that regulatory issues have come up only today, as many instances in the past reveal that the Indian vaccine PSUs have been made victims despite producing quality products. It is interesting to note that the OPV was indigenously prepared in PII Coonoor between 1967-1976 with the coordinated efforts of Government of India, World Health Organization (WHO) and Dr. Sabin, the discoverer of OPV vaccine. However, in 1976 the Government of India ordered PII to stop production alleging that some of the batches were found reactogenic. They samples were sent to the Haffkine Institute and facilities abroad for testing if they were virulent, just before the launching of EPI in WHO member countries. Since then OPV is one of the major imports among EPI vaccines until late 1990s [Madhavi 2007]. But later, it was found that the OPV batches from PII were perfectly safe and according to S. Archetti of WHO, that particular batch of Indian OPV were of excellent quality and the toxicology report of National Institute of communical diseases (NICD) was faulty [Ramachandran 2008]. It is intriguing to note that even then, the indigenous OPV production was not revived. There have been studies indicating

that the indigenous production is more economical compared to its imports [John 1981]. Yet, India opted for imported OPV on the advise of WHO. Similarly, one of the public sector vaccine institutes wanted to grow monkey kidney cell culture for the indigenous production of OPV, but they were discouraged on the advice of WHO and it was only in late 1990s that Haffkine Biopharmaceuticals (HBPCL) was allowed to obtain seed virus from abroad for its indigenous production. Once again in 2000, the Maharashtra State Government refused to buy OPV from HBPCL alleging that it was not potent, and procured OPV from Radicura Pharma, a private company. HBPCL had to file a PIL against the Maharashtra Government that it was a false allegation designed to favour a private company [Madhavi 2000]. Even the ultramodern GMP-compliant vaccine PSUs that emerged during post 1990s under the Department of Biotechnology faced regulatory hurdles, when UNICEF refused to accept OPV supplies from Bharat Immunologicals and Biologicals made from bulk imported from a Russian PSU, alleging that the vaccine from Russia was not WHO GMP compliant. India had no option but to import OPV bulk from Smith Kline Beecham (SKB) on the advice of WHO and only then was BIBCOL continues to function as a repackaging unit [Madhavi 2007]. Given this background, there is no guarantee that the emerging Hindusthan Health Care-led vaccine park at Chengalpattu would not meet the same fate as the other vaccine PSUs.

Media reports indicate that the real reasons behind the closure of PSUs were rather political than scientific and legal to promote vaccine private sector, and the reasons of WHO-GMP compliant comes in handy to kill the existing PSUs [Ramachandran 2008; Madhavi 2008]. It is also not very clear whether the newly set up private companies --- Green Signal Biopharma and Vatsan Biotech, Tamil Nadu --- that have benefited from these three PSUs for raw material, skilled manpower and finances (according to media reports) are WHO-GMP compliant! According to media reports, the Controller of Audit had raised serious objections regarding dubious financial dealings between the director of PII, BCGVL and the Green Signal Biopharma and Vatsan Biotech ltd., Tamilnadu, on the alleged corruption, favouritism, mismanagement and for not following procedural norms [Gopikrishnan, May 23d 2008]. It was pointed out by the 34th parliamentary standing committee on health, that the ministry did not take the offer of WHO to help in making these PSUs GMP complaint, rather it closed them and was not discussed in the cabinet before the units were closed (Rajya Sabha Secretariat 2009). Meanwhile, public health activists filed a public interest litigation (PIL) in view of the emerging child health crisis due to acute shortages of primary vaccines [Mudur 2009].

IV

Conclusion and Discussion

The President of India in her first address to the nation after the elections in May 2009, announced [Ray 2009], (backed up by health ministry's endorsement under its 100 days agenda) that the three vaccine units that were suspended in January 2008 would be reopened is welcome a step, though the fate of these PSUs is still uncertain as government is planning to introduce pentavalent vaccine (DTP-HB-Hib) in its national immunization programme [http://www.indianexpress. com/news/pentavalent-vaccine-likely-to-be-introduced/480971/]. Since PSUs do not produce pentavalent vaccine, government would procure pentavalent vaccine from private companies, making public sector's 70% of DTP production in the country redundant.

Secondly, the scientific rationality of introducing such combination vaccines under UIP becomes questionable and controversial as there is no unanimity among scientific community regarding its safety, protection efficacy and cost-efficacy in Indian population. Scientific evidence from India indicates that children develop immunity against Hib during infancy [Puliyel et al 2001].. Very few studies in India indicate that the incidence is very low in Indian population. [Minz et al 2009, IBIS 2002], Moreover, evidences from other countries show that in Hib vaccinated populations, some highly virulent Hib mutant strains are reported to have replaced the native strains [Bruce et al 2008, Lipsitch 1998, Muhalman 1996]. Hib vaccine induced Type 1 diabetes in children in some countries have been reported [Classen and Classen 2001 & 2002]. Srilanka launched pentavalent vaccine in its national immunization programme in Jan 2008 and in Oct 2009, SriLankan government suspended vaccination of pentavalent vaccine following four deaths after vaccination. [http://www.kuenselonline.com/modules.php?name=News&file=article&sid=13837]. Similarly, in Oct 2009 Bhutan suspended Pentavaent vaccination after 8 children died after vaccination[http://www.kuenselonline.com/modules.php?name=News&file=article&sid=14972], though WHO climed in NOV 2009 that these deaths were not due to vaccine[http://www.southasianmedia.net/index_story.cfm?id=618737&category=Frontend&Country=BHUTAN&pro=0]. These examples only underscore the need to establish the necessity, efficacy and safety of Hib vaccine in Indian population based on scientific evidence. from India Therefore, Hib vaccination becomes highly contentious and unethical, whether alone or in combination, without its proven efficacy and safety..

In general, the safety and efficacy aspects of combination vaccines are not proven beyond doubt [Girard 2005; Comenge & Girad 2006; Beri et al 2002, MIMS India

Nov 2009, Beeching et al 2004], and it is reported that they are less protective when compared to their individual components [FDA 1997; American Academy of Pediatrics 1999; Buttery et al 2005; Greenberg et al 2000; Kalies et al 2004; White et al 1997

In pentavalent vaccine (DTP-HB-Hib), lower immunological responses to Hep-B & HiB were observed when compared to their separate administration [Edwards & Decker 1997; www.library.nhs.uk/gastroliver; Pichicheo et al 1997; Jones et al 1998, WHO position paper on pertussis vaccines, 2005, Buttery et al 2005, Greenberg et al 2000; Kalies et al 2004; White et al 1997, Bar-On ES et al. 2009].

Combination vaccines do not have price advantage either. Most combinations, including the pentavalent vaccine, are not multivalent by design but are simple cocktails, which means that industry adds vaccines and multiplies prices. Pentavalent vaccine is costly, and may increase immunisation costs, as combination vaccines in general are more expensive than the existing primary vaccines. For instance, DTP vaccine that comes for Rs. 3 per dose from PSU and by combining DTP with Hepatitis B increases the price of DTP several fold (17-100 times fold) costlier [Madhavi 2006], indicating that the combination vaccines are nothing but meant for IPR and pricing advantages..

Worse, virtually every combination vaccine combines one of the universal vaccines with one or more of the new vaccines whose need for mass immunization has not been established beyond doubt. These are ingenious ways of 'value addition' invented by private sector in India and abroad marketing vaccines to increase its margins to sell to governments and individuals, just because they are available off the shelf.

If the pentavalent vaccine is introduced into UIP, the private sector will have no incentive to supply DTP at its original price (less than one-fiftieth the price of pentavalent), and will either stop selling it or increase the price of DTP substantially. Private sector refused to supply UIP vaccines at par with the prices of PSUs 6 months after the closure of the three PSUs, as it complined of loss in its revenue from vaccine sale. This experience with private sector during the suspension of 3 public sector units certainly indicates that the country cannot rely entirely on private sector for stable and affordable supply of UIP vaccines.Thus, pentavalent would adversely affect the DTP availability & pricing.

Introduction of Pentavalent vaccine in Indian UIP will kill PSUs even before revival, as pentavalent is produced only by private sector so far. Government purchase of pentavalent vaccine from private sector for UIP will deprive the PSUs of their earnings from DTP (their main source of income), while the government will waste public money

on buying dubious DTP+ combinations. The government should ban UIP and Non-UIP combinations to prevent market distortions and to meet shortages of the 6 UIP vaccines on priority basis.

Thus, introducing a pentavalent combination vaccine (DTP-HB-Hib) in UIP would be additional crisis, while country is not even prepared to set its house first, by resolving the current crisis of increased demand-supply gaps for UIP vaccines. One wonders why national governments have to pay money while private companies benefits at the cost of child health.

Thirdly, by over emphasising the logic of convenience in giving multiple vaccines together (often at the expense of lack of scientific evidence for their need, efficacy and safety), private companies have specialized in the art of adding vaccines and multiplying prices. This creates an artificial scarcity for affordable UIP vaccines, while the market is flooded with costly UIP-nonUIP combinations. It is estimated that the introduction of DTP-HepB in Indian UIP, would cost twice that of the national TB control programme [Madhavi 2006]. Combination vaccines are basically industry's ploy to capture UIP market that ensures future markets for their new vaccines through backdoor entry.

The current crisis of short supply for UIP vaccines must be resolved to ensure stable affordable supply of UIP vaccines as a priority by reviving and restrengthening Indian PSUs, and Indian indigenous capacity should not be compromised before introducing any new vaccine in Indian UIP. Several Indian studies indicate that many of the new imported vaccines may not be cost-effective and beneficial in Indian population keeping in view of epidemiology of prevailing diseases and protection efficacies of those vaccines [Phadke 2000; Arora and Pulivel 2005; Madhavi 2003, 2006]. Therefore, scientific, economic rationality and suitability must be established in Indian population, before introducing any new vaccines (and their combinations) in Indian UIP and these studies should be made transparent to win public confidence.

It is important to strengthen indigenous vaccine capacities not only to access universal vaccines, but also to tackle recent health emergencies such as swineflu. The recent emergence of swineflu in April 2009 and its spread in India, almost entirely from United States (US) originating passengers has prompted India to request the US to screen and retain outgoing passengers. While this could have retarded the spread, there have been embarrassing moments when patients ran away from the abysmal conditions in government hospitals in the national capital of Delhi and had to be brought back with police help. The state of the public health system in the country is far too well known,

notwithstanding government assurances that it is "fully prepared to tackle the situation". The ongoing battle against H1N1 (swine) flu has many lessons for developing countries already battling their ailing economies. One wonders whether Tamiflu (which was stock piled in case of emergent epidemic) would be protective against any future epidemic if H1N1 virus gets mutated. This also indicates that after all disease control is not about fire fighting against outbreaks, but of proper planning.

Table 8: Prices of Vaccines Produced by Public and Private Sector

Vaccine	**Quantity**	**Public Sector**	**Private Sector**
Primary (UIP) Vaccines		**(Indian Rupees)**	**(Indian Rupees)**
OPV	10ml	9.22	52.11
DPT	5ml	13.75	~ 15.00 - 215.00
TT (adsorbed)	5 ml	~2.40 to 5.12	37.50
TT	5 ml	2.68	5.83
DT	5ml	5.75	-
Measles	1 ml	None	~56.84 to 1125.
BCG	1dose		~10.00
New/Improved Vaccines			
Hepatitis B	Pediatric dose Adult dose	None	~45.00 to 181.00 ~190.00 to 345.00
DTP-Hepatitis B conjugate	Adult dose -	None	~97.00 to 225.00
R-Vac (against rubella)	1 dose	None	36.80
MMR	0.5ml	None	66.05
Anti-Rabies	0.5ml		~147.00 to 184.50
HAVRIX	1ml	None	~294.00 to 1125.66
(for hepatitis A)	Pediatric dose Adult dose		
	None	None	712.00 1360.00
Meningococcal A&C	Adult dose	None	1360.00
Influenza type B	1 dose	None	48.85 to 370.00
Typhoid	0.5ml	None	~185.00 to 400.00
HPV vaccine	1 dose	None	~3000.00
Anti-rabies vaccine	1 dose		~ 290.00 to 1112.50
Chickenpox	1 dose	None	~1430.00 to1500.00
Hib-TT	1 dose	None	~ 400.00
Source: Compiled from MIMS India 2008			

India must revive its indigenous capacities in view of price advantage (Table 8),and private sector should be made to meet national immunisation/health needs through

good governance and regulations. The presence of PSUs acts as a market deterrent to prevent monopolies in key areas of public health, make affordable products available for mass use (therefore saving the government health budget that goes into vaccine purchase), as well as to ensure health sovereignty (by avoiding imports or aid politics) and health security (biosecurity, biowarfare and defence concerns). Indigenous private sector can supplement and complement the government's efforts, but cannot be seen as a substitute.

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