Vaccines are important preventive medicines for primary health care, and are a critical component of a nation’s health security. Although international agencies such as the World Health Organization (WHO) and the United Nations Children’s Fund (UNICEF) promote global immunisation drives and policies, the success of an immunisation programme in any country depends more upon local realities and national policies (Box 1). This is particularly true for a huge and diverse developing country such as India, with its population of more than 1 billion people, and 25 million new births every year.

The current Indian market for vaccines is estimated to be about US$260 million [1]. India is among the major buyers and makers of vaccines, locally as well as globally, and has traditionally aimed at self-reliance in vaccine technologies and production. This article explores the trajectory of vaccine policy in India through its historical roots and institutional development, the gaps in demand and supply, the changing nature of the vaccine industry, and the emerging challenges in meeting national immunisation targets.

**Early Origins**

The history of vaccine research and production in India is almost as old as the history of vaccines themselves. During the latter half of the 19th century, when institutions for vaccine development and production were taking root in the Western world [2], the British rulers in India, concerned by the large number of their personnel dying from tropical diseases, promoted research on these diseases and established about fifteen vaccine institutes beginning in the 1890s. Prior to the establishment of these institutions, there were no dedicated organisations for medical research in India.

Haffkine’s development of the world’s first plague vaccine in 1897 (which he developed at the Plague Laboratory (Mumbai, India), later named the Haffkine Institute) and Manson’s development of an indigenous cholera vaccine at Kolkata during the same period bear testimony to the benefits of the early institutionalisation of vaccine research and development in India [3]. Soon, Indian vaccine institutes were also producing tetanus toxoid (TT), diphtheria toxoid (DT), and diphtheria, pertussis, and tetanus toxoid (DPT).

However, the benefits of this early institutionalisation did not last long. The policies of the colonial government ensured that Indian scientists were not a significant part of this intellectual legacy. By the time...
Indians inherited the leadership of the above institutions in the early 20th century, research and technological innovation were sidelined as demands for routine vaccine production took priority [3]. By the time India gained independence in 1947, the Indian vaccine research and development (R&D) institutions were no longer on a par with vaccine technology development centres elsewhere. This is reflected in the fact that improved techniques for bacterial vaccines were introduced in India almost a decade after their introduction elsewhere in the world (Table 1) [4].

What were the factors that led to the stagnation in vaccine development efforts between the time of Haffkine’s success and India’s independence? These included the pressures of routine production and service functions, financial constraints, lack of institutional mechanisms to foster and link up research and technology development, and the absence of an interdisciplinary approach. All these factors posed a threat to India’s vaccine development efforts [5].

### Vaccine Policy in Independent India

One year after its independence in 1947, India became a member country of the WHO and eagerly aligned itself to the policies of the WHO and UNICEF. Many new Indian institutions were established with partial support from international organisations during the period 1950–1970.

However, after independence, it took three decades for India to articulate its first official policy for childhood vaccination, a policy that was in alignment with the WHO’s policy of “Health for All by 2000” (famously announced in 1978 at Alma Atta, Kazakhstan). The WHO’s policy recommended universal immunisation of all children to reduce child mortality under its Expanded Programme of Immunization (EPI). In line with Health for All by 2000, in 1978 India introduced six childhood vaccines.

Table 1. The Introduction of Vaccine Technologies in India and Elsewhere in the World

| Vaccine      | Techniques of Production                                      | Year of Introduction | India | Elsewhere |
|--------------|---------------------------------------------------------------|----------------------|-------|----------|
| Smallpox     | Glycerinated vaccine lymph                                     | 1898                 | 1890s |
|              | Live attenuated freeze-dried vaccine                           | 1965                 | 1941  |
| Plague       | Whole-cell killed bacteria                                     | 1897                 | 1897  |
| Cholera      | Attenuated whole-cell preparation                              | 1892                 | 1892  |
|              | Agar-grown heat inactivated Vibrio cholerae whole-cell vaccine | 1911                 | 1902  |
|              | Cholera vaccine prepared using modern techniques              | Not yet              | 1996  |
| Yellow fever | Live attenuated (passing through cell lines) virus vaccine     | 1965                 | 1941  |
| Typhoid      | Heat-phenolized whole-cell vaccine                             | 1920                 | 1915  |
| Oral Typhoid | Heat-phenolized whole-cell vaccine                             | 1994 (Marketed by private sector) | 1994 |
| Rabies       | Dried cords of infected animals                                | —                    | 1885  |
|              | Glycerinated cord methods                                      | 1907                 | 1907  |
|              | Hogyes dilution method                                         | 1908                 | 1907  |
|              | 1% carbolysed rabbit brain vaccine                             | 1912                 | 1911  |
|              | 1% carbolysed sheep brain vaccine                              | 1930                 | —     |
|              | 5% carbolysed sheep brain vaccine (India used sheep to manage large-scale production) | 1933             | 1930 (prepared from rabbit brain) |
|              | 5% BPL inactivated sheep brain vaccine                         | 1959–today           | 1959 (prepared from mouse brain) |
| TT, DT, DPT  | Tissue-culture-based anti-rabies vaccine                       | 1977 (SII)           | 1977  |
| TT           | Purified toxoids inactivated with formaldehyde                 | 1920s                | 1920s |
| DT, DPT      | Purified toxoids adsorbed to aluminium phosphate               | 1972                 | 1963  |
| Bacillus Calmette-Guerin | Liquid bacterial vaccine                                    | 1951                 | 1927  |
|              | Freeze-dried bacterial vaccine                                 | 1967                 | 1960s |
| IPV          | Inactivated polio vaccine (discovered by Salk)                 | 1984 (SII)           | 1955  |
| OPV          | Monkey kidney cell culture vaccine                             | 1967                 | 1962  |
| Improved IPV | Vero cell culture techniques                                   | Marketed by private sector | 1988–1989 |
| Measles      | Tissue-culture-based vaccine                                   | 1989                 | Late 1980s |
| Hepatitis B  | Recombinant DNA technology                                     | 1997 (Shanta Biotech, Hyderabad, India) | 1980s |

Source: [4].
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1977 with the help of seed virus from polio vaccine during the period 1967–1971 to 2001, the Ministry of Health and Family Welfare (Government of India) and MIMS India (www.mims-india.com), Nov 2001, New Delhi.

(Measles vaccine was added much later, in 1985, when the Indian government launched the Universal Immunization Programme (UIP) and a mission to achieve immunisation coverage of all children and pregnant women by the 1990s. The failure of the Indian public sector to recover from its mounting failures to achieve self-sufficiency and self-reliance in primary vaccines is also related to the liberalisation and globalisation of the Indian economy. It is not a coincidence that these failures and closures, and the preference for imports (while paying lip service to self-reliance), happened after the Indian government liberalised its economy in 1991 as prescribed by the International Monetary Fund and the World Bank. It is no longer fashionable to produce vaccines in the public sector in India, let alone to try and revive failing public sector units, even if essential vaccines are not available from the private sector.

The Increased Role of the Private Sector: Distorted Prioritisation of Vaccine R&D/Production

One of the main reasons for the growing gap in demand for and supply of primary vaccines in India is that while public sector production is on the decline (Figure 1), vaccine availability from the private sector (Figures 1 and 2) or through the UNICEF procurement mechanism (based on global tenders from suppliers pre-approved by the WHO) has not improved. This is a part of...
a worrisome global trend that has been acknowledged by UNICEF (http://www.unicef.org/supply/index_vaccine_security.html).

Shortages of primary vaccines in developing countries began to emerge in the late 1990s. These shortages were due to the introduction of new, more sophisticated, more expensive vaccines in industrialised country markets, leading to manufacturers phasing out the production of the traditional, less expensive vaccines used in developing countries. Between 1998 and 2001, ten out of 14 major manufacturers partially or totally stopped production of traditional vaccines. Eight of these firms were the main suppliers of vaccines to UNICEF. Of these eight, six were involved in mergers between larger pharmaceutical companies. The overall outcome of these developments is that the availability of primary vaccines to UNICEF has dramatically decreased, while the prices have increased (http://www.unicef.org/publications/index_4442.html).

Indeed, the rapid growth (8%–10% per annum) of India’s current human vaccine market is mainly attributed to the new, high-priced vaccines (Figure 2 and Table 2) such as Hepatitis B that have been launched since the 1990s. There has been pressure from the industry to include these new vaccines in the government’s UIP, even though the clinical and epidemiological justification for their inclusion is controversial [9,10]. With epidemiology taking a backseat, government decisions on vaccination are increasingly determined by price competition and supply “push” (by the companies) rather than “pull” (demand) from proven public health needs [9].

Many western countries have included several other new vaccines (such as influenza type B, meningitis, measles-mumps-rubella, and chickenpox) in their regular immunisation programmes [11]. These trends are used as a justification by the industry to include these vaccines in the Indian UIP in the future. Aggressive promotional campaigns for the new vaccines and their quick adoption by industry-friendly private medical practitioners have already made these vaccines akin to fast-moving consumer goods. The industry, which enjoys all the benefits of economic liberalisation, sees no contradiction in seeking a captive market for its new vaccines through the government-sponsored UIP while at the same time failing to meet its social responsibility to meet the shortfall in production of existing UIP vaccines.

There is another serious contradiction that grips the global drug and vaccine industry. For curative medicine, the pharmaceutical industry places increasing emphasis on the use of genomics and bioinformatics to move toward customised medicine to suit different populations. And yet in vaccines, the tendency is to move toward a “one vaccine fits all” regime. This would be fine if the vaccines were specifically designed for universal use, but there was no attempt to conclusively establish that the imported vaccines actually suited the Indian strains of the pathogens before they were adopted. Doubts over suitability that have subsequently emerged have not been adequately addressed. With the decline of epidemiology and disease surveillance in India, and the main emphasis being on the statistics of vaccine “coverage” rather than the immune protection achieved, it seems that spending money on vaccines is more important than actual disease prevention. If these trends continue unabated, they will lead to serious distortions in the vaccination programmes of India and other developing countries facing a similar situation.

Conclusions and Recommendations

India enjoyed the advantages of early initial successes in vaccine R&D and indigenous production in the public sector, but the country is increasingly unable to cope with the growing gap in the demand and supply of UIP vaccines [6]. The availability of UIP vaccines from the private sector is also on the decline in India and abroad,

### Table 2. Cost of Full Immunisation with Each Vaccine (in US dollars)

| Category                      | Vaccine                        | Quantity  | Public Sector | Private Sector |
|-------------------------------|--------------------------------|-----------|---------------|----------------|
| Primary vaccines under EPI    | OPV                            | Three doses | 0.03          | 0.16           |
|                               | DPT                            | Three doses | 0.08          | –0.09 to 1.34  |
|                               | TT (adsorbed)                  | Two doses  | –0.01 to 0.02 | 0.15           |
|                               | TT                             | Two doses  | 0.01          | 0.02           |
|                               | DT                             | Two doses  | 0.02          | –0.59 to 11.69 |
|                               | Measles                        | One dose   | None          | –2.80 to 11.30 |
| New/improved vaccines         | Hepatitis B                    | Paediatric | None          | –6.05 to 9.35  |
|                               | DTP-Hepatitis B conjugate      | One dose   | None          | –6.79 to 14.03 |
|                               | R-Vac (against rubella)        | One dose   | None          | 0.76           |
|                               | Measles-mumps-rubella          | One dose   | None          | 1.37           |
|                               | Anti-Rabies                    | Three doses, prophylaxis | –18.33 to 70.20 |
|                               | HAVRIX (for Hepatitis A)       | Six doses, post-exposure | –36.67 to 140.41 |
|                               | Adult                          |            | None          | 14.80          |
|                               | Meningococcal A&C              | One dose   | None          | 28.27          |
|                               | Influenza type B               | Three doses | None          | 1.01           |
|                               | Typhoid                        | Three doses | None          | –23.07 to 24.94 |
|                               | Chickenpox                     | One dose   | None          | 27.96          |

Data compiled from Monthly Index of Medical Specialities (MIMS) India, New Delhi, November 2001.
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in favour of more expensive new vaccines and combination vaccines, whose public health need has not been unequivocally established in India with sound epidemiological and cost-benefit data [9,12]. Therefore, India (and indeed, every country) must evolve its own national strategies to meet its vaccination needs within its budgetary constraints. To do so will require four key actions.

The first and foremost element in this strategy must be the decisive intervention of the Indian government to meet the shortfall in the UIP vaccines. This may be done either by strengthening the public sector wherever possible, or by taking suitable (and transparent) measures to encourage the indigenous private sector on a case-by-case basis to make safe and effective vaccines available at affordable prices. The suitability of imported vaccines to deal with Indian pathogenic strains also needs to be conclusively established wherever necessary. The health security of a nation of India’s size cannot be left to the vagaries of global market forces. With a strong will and a small amount of planning, the current situation in India can be reversed, and India can even play a major role in meeting the global shortfall in the vaccines procured by UNICEF.

Secondly, India needs to strengthen epidemiology and revive the collapsing disease surveillance system. This would help to decide between universal or selective immunisation based on unequivocal scientific evidence, as well as to respond to the changing disease prevalence scenario on the ground, which may call for a move from universal to selective immunisation or vice versa. Some diseases may not need vaccinating against at all, and may be better controlled by other strategies, such as better sanitation, vector control, quarantine, and curative medicines. National immunisation programmes must be led by scientifically established public health needs and not by the mere availability of a vaccine in the market.

Thirdly, a strong emphasis on in-house R&D is needed in order to ensure that our production technologies are in tune with the times, and to negotiate strategic partnerships with outside scientists or institutions and companies.

Last but not least, the Indian government should actively encourage independent policy research, cost-benefit studies, and wider national consultations on various aspects of vaccination and public health so that it can take more informed decisions on such matters.

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