Agenda Setting in Vaccine Policy and Social Relevance of the Emerging Vaccine Technologies from Public Health Perspective – PART 1

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ABSTRACT

Vaccine technologies have remained a favorite tool for the techno-centric policy establishment to address the morbidity and mortality burden of disease while neglecting comprehensive social, economic and health systems development. Even as implementation of immunization for six primary vaccines remains far from optimal, misplaced arguments are furthered for introduction of newer vaccines. Policy on vaccines in India has tended to be swayed by unhealthy considerations that are extraneous to an epidemiological approach.

The paper examines relevant literature to highlight the factors shaping the country's vaccination policies; discusses methods for optimal cost benefit analysis of vaccines, and proposes desirable criteria of an epidemiologically guided vaccine policy. For newer vaccines, public health burden of the targeted diseases, their epidemiology, possible ways of ameliorating the disease burden are chronicled to evaluate the desirability of these vaccines in the current scenario. Rota virus vaccine, the Hib pentavalent vaccine and the HPV (Human Papilloma Virus vaccine) are discussed.

The paper is organized in two parts. Part 1 deals with the influences guiding vaccine policy and the percepts of a scientific vaccine policy. Part 2 discusses the case studies of Rota virus and Hib pentavalent vaccines; the two vaccines being intensively targeted for inclusion.

There is a structured impetuousness on part of the pro-vaccine lobby to push for the inclusion of newer vaccines, without adequate regard to epidemiology and feasibility. Accordingly the paper argues against adoption of these vaccines in public health programs under the present circumstances.

Key words: Immunization, vaccine, Rota virus, Hib

INTRODUCTION

Vaccines are considered a cost effective technological intervention for prevention and control of communicable diseases. The dominant development paradigm adhered to by policy makers in developing countries, donor agencies and organizations like W.H.O and UNICEF, argues for well planned technological interventions to overcome the drawbacks of poor socioeconomic development in developing countries for achieving better health standards. This prioritizes technology packages over comprehensive health systems development.[1] Vaccines are faster developing technological tools against the emerging and re-emerging communicable diseases, and as such the lure of their perceived potential has only become stronger. The activism of drug industry and increasing convergence of interests between philanthropic, technical and civil society organizations dedicated to adoption of newer vaccines globally has made decision making process regarding vaccines contentious.

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This paper elucidates the factors impacting upon the agenda setting in vaccine policy and social relevance of some newer vaccines current on the public health agenda among which Rota Virus vaccine and vaccine against Haemophilus Influenza (Hib) are being discussed.

CURRENT SCENARIO OF VACCINATION PROGRAM IN INDIA

Foregoing discussion sets the field for assessing some of the newer vaccines current in the public health debate in India. It need be known here that currently the government of India spends upwards of Rs 200 crores (approx. 45.5 million US dollars) annually on the six vaccines included in the UIP i.e. BCG, DPT, Polio, Measles, DT and TT. Expenditure on Pulse Polio Program is not included in this. Immunization program manages to reach only about half of the 26 million children born in the country every year.[2]

After the 1980s the public sector supply of EPI vaccines has fallen steeply despite the official rhetoric of achieving self-sufficiency in vaccine production in the country. With 10 out of 14 major producers stopping manufacture of traditional vaccines, procuring vaccines even from the private sector has become difficult since 1990s. Around 8 of these companies were official suppliers to UNICEF.[3] With public sector no more being the mainstay of cheap primary vaccines, the government has to depend on private players who invariably provide combinations of newer vaccines with the primary vaccines, which not only increases the cost but also distorts the schedule of the vaccination program.

UNHEALTHY INFLUENCES OVER VACCINE POLICY

Emphasizing the role of the international agencies in setting the global agenda for vaccines Greenough and Streefland have said:

'Vaccine technology represents a biomedical intervention with truly global ramifications. Strategic policy formulations, target setting and prioritization in funding have become transnational processes with a wide range of actors orchestrated by global actors such as Child Vaccine Initiative. Though the implementation of vaccination programme is a national endeavor, the transnational decision-making has become an integral part of public sector health service delivery."[4] In 1991 only 30 countries around the world manufactured vaccines. Only six were from developing world, including India; rest were either from the West or from the erstwhile Socialist block[5] The developing world is thus dependent on the developed countries for their vaccine demand.

India, an early starter in vaccine technologies was at par with the World by 1930s; even though this head start resulted from British colonialism's own strategic needs. From 1940s India fell far behind the West in developing vaccines, and by the time of biotechnology revolution of the 1970s we lagged far behind.[5] India's vaccination policy post 1947 has displayed little initiative and ingenuity; dovetailing the international policy prescriptions to the extent that even the existing infrastructure has been allowed to go waste; ostensibly to benefit the foreign interests.[5] The globalization and free market policies have further degraded country's indigenous capabilities.

The Union Ministry for Health and Family Welfare (MOHFW) ordered closure of public sector undertakings producing cheap vaccines for country's immunization program for dubious reasons.[6] On June 19, 2007, the then Union Health Minister, Dr Anabumani Ramadoss lavished praise on the scientists of the Pasteur Institute of India for their services in saving millions of lives in the country; yet seven months later the license of the Institute for vaccine production was cancelled along with that of two other public sector units, ostensibly under pressure from the WHO. It was alleged said that the institutions had failed to comply with the current Good Manufacturing Norms under the Indian Drug and Cosmetic Rules. Yet, the licenses of these units were revoked without any 'corrective measures' having been taken to remove the alleged shortcomings.[6] The Javaid Chaudhary Committee that enquired into the matter remarked of the government's conduct:

"The only conclusion that the committee can draw is that the Ministry, at its highest political and bureaucratic levels, was associated with the final decision for the closure of the units. Thus, the constructive responsibility for the final decision would also rest on the apex functionaries of the political and bureaucratic executive, including the Union Minister for Health and Family Welfare and the then Union Health and Family Welfare Secretary."[6]

The acts have made the country vulnerable to pressures and manipulations of 'Transnational Alliances for Vaccines', which came into being in the 1990s i.e. during the globalization era. Table 1 below summarizes the objectives of some of these alliances:

Table 1: Transnational (Global) Alliances for Vaccines.

Alliance	Year of launching	Objective	Sponsors
Children Vaccine Initiative (CVI)	1990	To develop global strategies for development & utilization of vaccines	UNICEF, WB, UNDP, WHO, RF, World's largest manufacturers and the marketers
Global Programme on Vaccination (GPV)	1990	New vaccine development program to purchase and supply vaccines to EPI	Sponsors of WHO
International AIDS Vaccine Initiative (IAVI)	1996	To develop antivirals against HIV for the world. Encourages industry participation and supports vaccine development partnerships.	Governments of UK, Netherlands and Canada, WB, the Bill and Melinda Gates Foundation, RF, Sloan Foundation and Starr Foundation.
Medicines for Malaria Venture (MMV) – an entrepreneurial non-profit international organization-	–	To create incentives to develop new drugs & vaccines. To improve private sector participation and to eradicate malaria burden by 2010. To supply vaccines at cheaper prices to poor countries.	RF, WB, SKB, Wellcome Trust, DFID, IFPMA, The Association of British Pharmaceutical Industries, Philanthropic donations & Foundations.
Global Alliance for Vaccines and Immunization (GAVI)	1999	Every child in the world would be protected against vaccine preventable diseases.	Bill and Melinda Gates Foundation, IFPMA, Public health and research institutions, national governments, RF, UNICEF, WB, WHO.
Malaria Vaccine Initiative (MVI)	1999	To accelerate and develop vaccine candidates against malaria. To ensure their accessibility to developing world.	Bill & Melinda Gates Foundation.

Source: Y Madhavi. Asian Biotechnology and Development Review, 2007; Vol. 9 (2): p 1–43.

Note: WB = World Bank, RF = Rockefeller Foundation, DFID = Department for International Development (Government of UK).

Table 1 shows considerable cooperation between Western transnational corporations, the governments of these countries and the donor and technical agencies like the World Bank, UNICEF and the WHO, in shaping the immunization programs World over. Negligible contribution by the developing countries to vaccine production or finances ensures that they have little say in the decisions of these alliances which are readily sanctified by WHO and UNICEF and are taken as given.

Dominance of GAVI by the Bill and Melinda Gates Foundation make it by far the largest contributor to vaccination programs. It has substantial business interests in at least nine pharmaceutical majors; its representative sits on the Board of the Global Fund to fight AIDS, tuberculosis and malaria and the Chief executive of Merck was earlier on the Board of Microsoft. The Foundation exercises considerable influence over India's health policies. It sponsored the Commission on Macroeconomics and Health which held the protection of intellectual property as crucial to investment in drug development and research and also the report prepared by Indian Council for Research on International Economic Relations that recommended the setting up of world class schools of public health in India. PHFI (Public Health Foundation of India; a public-private partnership) was set up soon thereafter and the Gates Foundation has intimate association with PHFI.[7] Foundation's inroads into mechanisms for leveraging policies in favor of newer vaccines are deep.

Placing the Global Alliances for Vaccines in Perspective

Vaccine development is a costly, high risk and incurs long gestation period.[8] Huge proportion of vaccine markets exist in the developed world with US alone accounting for 60 % of global profits.[9] The research and development of vaccines thus becomes directed primarily by the needs of the developed countries. Lesser profitability from demand for cheaper primary vaccines from developing countries propels companies to shift to newer vaccine technologies. Strong 'pull' (a clear cut assured demand) and 'push' (technical and operational feasibility) factors are required to get major vaccine manufacturers interested in the less profitable third world markets. Lower profitability of vaccines is due to their one time use in the life; persistent uncertainties in the market demand from developing world depending upon expansion of coverage in these countries.[10] It is in this context that the role of UNICEF, WHO and foundations like the Bill and Melinda Gates becomes important.

"Through global inputs and interventions of United Nations (UN) agencies and alliances such as GAVI, immunization programs in the developing world are

becoming better financed."[10] This is getting reflected by way of:[10]

1. "A better defined value of immunization in economic terms"
2. "More funds available at country level."
3. "Greater emphasis on adding new products into national programs" and
4. "More *responsible* behavior on the part of countries receiving vaccines."

That the utilization of finances ought to be guided by the epidemiologically determined need for a vaccine is however not emphasized. "More responsible behavior" is but a euphemism for unquestioningly following the transnational dictates. Epidemiology is further marginalized in immunization programs by the manner in which WHO defines sustainable vaccination:

"the ability…to mobilize and efficiently use domestic and supplementary external resources on a reliable basis to achieve current and future target levels of immunization performance in terms of access, utilization, quality, safety and equity."[11] It seems resources alone suffice to make a sustainable vaccination program independent of epidemiological tenability. Further, a country will be deemed to be behaving 'irresponsibly' upon refusing to commit domestic resources desired of them or for refusing to implement conditions attached to 'supplementary external resources'. WHO and researchers like David Bloom have developed next logical line of argument to facilitate 'responsible' behavior – good health is necessary for development and "Vaccines in particular…are an inexpensive and extremely effective means of improving health and overall welfare. Their impacts…are much greater than previously thought…and policy makers who neglect immunization will be missing a great opportunity for promoting development."[12]

Proponents of this "great opportunity for promoting development" ignore the fact that "the demand for this initiative did not emanate from the designated beneficiaries. Rather, the countries as a group have had to be wooed, *educated* (emphasis ours), and financially enticed to accept the GAVI's goals as their own."[13]

Rather than being 'facilitators' in achieving health goals, the problem with initiatives like GAVI is that they become 'movers and shakers' in imposing their goals. GAVI has resisted transfer of vaccine manufacture technology to third world countries possibly to keep the interests of transnational corporations secure.[14] Only a small fraction of GAVI's aid is actually for strengthening coverage for six primary vaccines, while the thrust is on introduction of the more sophisticated vaccines.[15] Together with prioritization of private sector funding these policies undermine self reliance in vaccine technologies by the developing countries while jeopardizing sustainability of vaccination programs.[16]

DESIRABLE STRATEGY FOR INCLUSION OF A VACCINE IN IMMUNIZATION PROGRAM

There are myriad influences impacting the inclusion of vaccines in the vaccination programs. Undermentioned are some important principles to guide the approach towards newer vaccines:

- Vaccines are not a substitute for measures like good nutrition, safe water, environmental sanitation, poverty reduction comprehensive health care, improvement in educational standards and empowerment of women.[17] [18] Though easily stated, these measures are not easily prioritized in policy.
- An epidemiological approach that takes into account the burden of disease compared to other health problems, extent to which the disease epidemiology lends it to control through vaccination, the possibility of more serious infections due to strain replacement consequent to introduction of vaccination and the impact of vaccination on co-morbidities with similar epidemiological profile, should be primary in guiding policy. Ongoing 'Polio Eradication Program' is a good case in the point – even as there are contending views regarding how much of a public health priority polio was for the country; its epidemiology does not lend it amenable to eradication through vaccination, besides the fact that the consequences of such unprecedented levels of polio vaccination to the epidemiology of the disease remain unknown.[19] The distortion of public health priorities such programs can cause is evident from the fact that in today's time the pulse polio immunization program is consuming more resources than those spent on immunization against the five other diseases of UIP; besides causing disruption of even routine functioning of the peripheral health services at a cost that cannot be measured only in

economic terms.[20] Interestingly some of the more important bottlenecks that have been identified in the eradication of polio include – levels of routine immunization that remain very low and deplorable environmental sanitation coupled with high prevalence of non-polio entero-viruses which necessitates unprecedented levels of polio vaccination to achieve sero-conversion.[21] [22]

- For therapeutic vaccines and anti-sera for tetanus, diphtheria, anti-snake venom and anti-rabies, recipients shall only be those suffering from these conditions;[23] [24] all other vaccines should only be targeted for selective vaccination unless scientific evidence mandates their universal delivery [25] [26] [27] Even universal vaccines may be unequivocally defined as such only in the context of children and pregnant women;[28] [29] for adults there should be a selective approach for at risk individuals only.[30] [31] This is important in the context of the push for inclusion of many vaccines as part of the Universal Immunization Program (UIP).
- Maximizing coverage with the six primary vaccines (BCG, DPT, Polio, Measels, DT and TT) should remain the priority. Inclusion of a new vaccine should not compromise primary immunization. Irrational vaccine combinations, especially those combining non-UIP vaccines with the primary (UIP) vaccines should be discouraged as this increases the cost of vaccines and is a way to push newer vaccines through the back door.[32]
- Cost benefit should go beyond the conventional accounting for cost of procuring vaccines, cost of their delivery and the money saved by reducing the incidence and prevalence of disease that the vaccine may bring about. Developing indigenous capability for producing desirable vaccines reduces the cost of procurement while ensuring its availability on a sustainable basis free from vagaries of market dynamics.
- Vaccine viability under adverse conditions like higher temperature; convenient administration not requiring skilled man power e.g. oral administration vis. a vis. injectable forms; amenability to combined dosage with other vaccines without compromising immunogenic response; opportunity costs to the consumers; iatrogenic costs due to interaction with other drugs; environmental costs due to disposal of wastes like the plastic syringes; cost of continuing research into changing behavior of the pathogen on account of vaccination, immunogenic profile of the people before and after vaccination against the locally prevalent strains of the pathogen and the health systems research for improving the delivery of vaccines to attain a wider coverage are some other factors to be considered while making the cost benefit analysis. Figure 1 gives the schematic representation of these factors.
- Vaccine that is a little less efficient under lab conditions than another vaccine against the same pathogen, but lends itself to easier production, greater stability of potency under field conditions and convenient administration, and thereby a wider coverage may prove to be more cost effective from public health point of view.

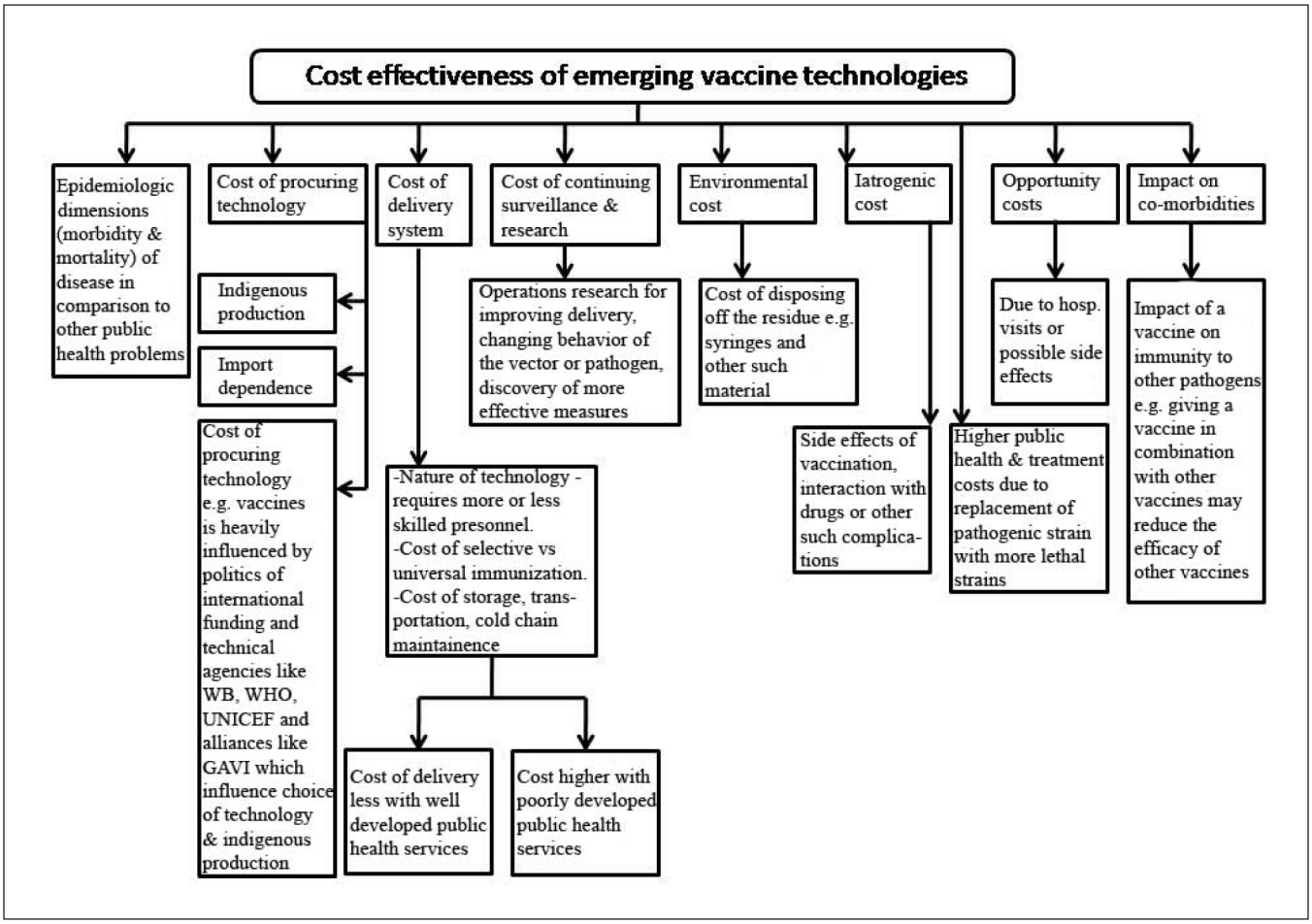
A COMMENT ON THE DRAFT NATIONAL VACCINE POLICY, 2011

At long last a formal vaccine policy has been put in place by the Ministry of Health and Family Welfare in 2011. This would indeed be a welcome development if the policy is able to give an epidemiologically sound rationale to vaccination program in the country. It would only be in the fitness of things that we examine here some of the pertinent features of this policy document in light of the foregoing discussion.

Vaccines are no doubt a powerful weapon in the fight against communicable diseases; however, their potential is best realized only if the role of vaccines is rightly placed in the context of other factors that impact on the burden of disease. There is overbearing evidence to show that major decline in the burden of communicable diseases World over occurred with improvement in socio-economic conditions of the people which enabled better nutrition and healthier conditions of living. Vaccines came much later in the picture.[33]

Even though newer vaccines have become available, still the classical 'vaccine preventable diseases' account for a very small percentage of the overall infant and under five mortality.[34] Having said this, it is also true that achievements like eradication of small pox; or elimination of communicable diseases from large parts of the World may not have been possible without the help of vaccines.

These observations can hardly be taken as widely understood and need be clearly emphasized in a policy document as a guide to contextualizing vaccines as a



public health intervention for reducing the burden of disease vis-à-vis other interventions like proper nutrition, safe drinking water, environmental sanitation and overall health systems development; among the oldest and most enduring ideas in public health.[1] These can hardly be overemphasized at a time when there is a continuing infatuation with the belief that vaccines are a quicker and more cost-effective way to overpowering disease. Projecting the achievements of its immunization efforts in the 'Comprehensive Rural Health Services Project, Ballabhgarh' in the State of Haryana, a paper from the country's most prestigious medical institution boastfully proclaimed in its title – "Development is not essential to reduce infant mortality rate in India" and went on to suggest that "The Kerala model, which focuses on social development, may not apply to northern India."[35] The entire experience of 'pulse polio' program which emphasizes immunization as the sole strategy and has missed one deadline after another for proclaiming the elimination of disease from India; is a living example of this flawed thinking.

The 2011 draft 'National Vaccine Policy' fails to emphasize the need to correct this flawed orientation towards the use of vaccines; rather, the policy propagates it further. In the 'Policy Context and Framework' section, it is stated:

"There are a number of new vaccines, which have become part of National Immunization Programs (NIPs) in many developing and developed countries. Many a times, the decision to introduce these vaccines is delayed due to limited production capacity…….Sometimes vaccines are not used as these are not indigenously produced or not available in sufficient quantity. On the other hand, the manufacturers don't produce vaccine because these are not used in the program."[36]

It further states in the section on 'Situation Analysis' – "For almost two decades since the beginning of UIP, India has had the same 6 antigens in the UIP…….a number of new vaccines have become available in the last few years. Hemophilus influenza type b (Hib) vaccines, Pneumococcal conjugate vaccines, Rotavirus vaccines,

HPV vaccines, which have estimated high burden and possible role in reducing child mortality in India."[36]

Unless put in proper perspective these facts by themselves have the potential of further encouraging the prevalent uncritical approach to the use of vaccines. For example the policy proposes to make it "mandatory for Government to support developments with Advance Market Commitments and honor the commitments and setting up a Vaccine Fund through 'innovative financing mechanisms, for introducing new vaccines…"[36] On face of it, it amounts to assuring profits for private vaccine manufacturers at the cost of public exchequer and such prescription is loaded with tremendous conflicts of interest, consequences of which go far beyond econometrics alone.

Promoting and facilitating vaccine research and development is one thing, but commitment towards adoption of a vaccine in the immunization program can only follow its being established as a cost-effective intervention in the given field conditions. The term 'effective' is also to be defined very carefully. Often time studies reporting relative risk reduction of a disease in immunized persons are considered as the valued evidence base for decisions recommending a vaccine. Relative risk reduction i.e. percentage reduction in the risk of disease with vaccination tends to artificially magnify an otherwise modest risk benefit. Absolute risk reduction (difference between risk of disease in non-vaccinated and risk of disease in vaccinated), and the numbers need to treat (NNT) are a much more desirable statistic in this respect. These coupled with numbers needed to harm (NNH; used for assessing side effects) for a vaccine are a must for having a better idea of the cost-effectiveness of a vaccine.[37] Apart from this we need to factor in all the other factors relevant to cost effectiveness analysis that have been discussed earlier in the article. Likewise we need to weigh these considerations for each of the alternative interventions before a decision can be reached.

Doing all this is no mean task and requires a formidable research base and regulatory mechanisms. That the concerned research gives us reliable results on which people's welfare can be staked requires that it should be free from any conflicts of interest. Influential bodies like the Indian Academy of Pediatrics (IAP) occupy pride of place in NTAGI (National Technical Advisory Group on Immunization). The multifarious links of such bodies of medical professionals with the industry are only two well known. With the IAP's Committee on Immunization (COI) expressing its intent of initiating "collaborative projects with other agencies, NGOs and vaccine manufacturers"[38] its conflict of interest has only become explicit. How will these conflicts of interests be resolved? What shall be the processes for ensuring an epidemiologically guided and transparent decision making process? In the prevailing environment of corporate greed, there perhaps is a need to even consider legally binding mechanisms for such process. These are some of the formidable challenges before the country and ought to have been illuminated in the draft vaccine policy, especially as the present state of affairs leaves much to be desired in this respect.

Most regrettably, the present policy does much the reverse; it rather invites conflict of interest. 'Vaccine Research and Development' is seen as a "tremendous economic opportunity", arising out of growing vaccine manufacturing sector and fast increasing global demand in vaccine R & D by exploring the linkages with international institutions such as the Gates Foundation, GAVI and PATH among others.[36]

The foregoing sections of this article have already discussed the role of these international foundations / NGOs in exercising a pernicious influence over the immunization programs in different countries. It is amazing that the policy does advocacy for collaboration with international NGOs like PATH despite their more than condemnable role in the HPV trials in the country.

Besides, emphasizing exploiting "tremendous economic opportunity" and linkages with industry internationally lends the vaccine program amenable to the influence of international market which has the potential of destabilizing even the basic immunization program in the country. The policy document itself brings out the facts that while on one hand Indian manufacturers provide 43% of global vaccine supply; on the other hand the national average for coverage of the six UIP vaccines is less than 50%.[36] There is less than adequate attention paid in the policy document to address such anachronisms in the vaccine program of the country.

It has been noted above how the institutional capacity in the public sector to meet the requirements of basic vaccines for the country's immunization program was undermined through a series of circumspect decisions. The private sector on its part has been unwilling to provide the cheaper UIP vaccines without combining them with the costlier newer vaccines which are not included in the UIP. A logical policy directive to this would have been to strengthen the institutional capacity in public sector.

Once the primacy of the public sector is established in the field keeping in line that the primary objective of 'Vaccine Research and Development' is larger human welfare, the 'tremendous economic opportunity' may be explored as a secondary objective. Unfortunately, the policy fails to lay the road map for the revival of public sector capacity in vaccines, except for suggesting the management of the public sector to be developed along the lines of private sector.

An epidemiological approach which includes the specific epidemiological features of a disease is the fundamental premise of this paper for developing vaccination strategies against a disease. The "Criteria for selection of vaccines for introduction" given in the vaccine policy document touch upon disease epidemiology only to the extent of mentioning – "Disease burden (incidence / prevalence, absolute number of morbidity / mortality, epidemic / pandemic potential)"[36] as a criterion for inclusion of vaccines; consideration for pathogen, host and environmental interactions and long term impact of vaccination on disease epidemiology have simply gone missing.

The 'vaccine research and development' ought to go far beyond vaccine development and vaccine trials. A comprehensive research and development policy has to include areas like assessing the burden of disease and operations research to continuously improve the vaccine delivery. There needs to be an institutional mechanism for this. Policy directions in this regard could prove immensely beneficial for improving the coverage of the vaccine program in the country, but there is little deliberation on these aspects in the policy.

Recommendations like the 'Creation of bio-repositories', surveillance systems for 'Adverse events following immunization (AEFI) and Vaccine preventable diseases (VPDs) and the development of human resources to support research and development of vaccines and implementation of vaccination programs are definitely positive, but with the crux of the matter being compromised, these are mere fillers.

We conclude here part 1 of the paper. The second part shall deal with the case studies of Rotavirus and Hib pentavalent vaccine.

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