OPPI Position Paper on Vaccines

Background

There is no other health intervention as simple, powerful, and cost-effective as a ‘vaccine’. Vaccines currently prevent more than 3 million deaths per year, and the positive economic impact is in excess of a billion dollars per year. During the 20th century, the average human life span has increased by approximately 30 years, a significant portion of which has been attributed directly to vaccination. Though vaccines have transformed public health throughout the world, for children in particular, the burden of vaccine-preventable diseases in India is still substantial and hence the usage of this powerful tool is still not optimal in our country.

Different stakeholders like Ministry of Health and Family Welfare, National Technical Advisory Group on Immunization (NTAGI), Indian Council for Medical Research (ICMR), UNICEF and Vaccine manufacturers (Developing Countries Vaccine Manufacturing Network (DVCNMN) which supplies 40% of the world’s vaccines, and top multinational vaccine manufacturers) play an important role for introduction of Vaccines in India. The queuing process in place for vaccine introduction and the fact that immunization coverage and cold chain may be skewed towards polio vaccination, has affected routine immunization. Each year twenty-seven million new births take place in India, which is the largest birth cohort in the world. Out of these, children fewer than 44 percent receive the full immunization schedule. Differential policy efforts between states and major improvements in outreach in urban and rural areas have led to a drop in percentage of children receiving no immunization and increase in heterogeneity of immunization rates in rural areas (Gaudin and Yazbeck 2006). The problem that has to be dealt with is stagnation in full immunization rates juxtaposed against a growing, vibrant vaccine industry in India.

OPPI’s Position Paper on Vaccines comprehensively covers issues related to immunization, as follows:

(1) Value of Vaccines
(2) Regulatory Environment
(3) Vaccine Policy for Improving Vaccination Coverage
(4) Strengthening Immunization Infrastructure
(5) Vaccine to Vaccination and
(6) Innovative Financing.

Our conceptual formation perspective in priority setting of issues in vaccine introduction is an “accountability for reasonableness” approach, where interface with regulatory
authorities would involve (i) transparency on the basis of any decisions taken (ii) scope for appeals to rationales that can be accepted as relevant to meeting health needs in a fair manner and (iii) procedures for revising decisions in light of challenges to regulatory decisions taken (Daniels 2000).

(1) Value of Vaccines

The impact of vaccination on the health of the world’s people is difficult to exaggerate. No other modality, except sanitation and safe water, has had such a major effect on mortality reduction and population growth (Plotkin and Plotkin 1988)

- Disease Eradication and Prevention
  The prevention of diseases by vaccination is without question one of the most significant medical achievements of mankind. Vaccines currently prevent more than 3 million deaths per year. One infectious disease, smallpox, has been eradicated by vaccination, and another, polio, is on the verge of eradication. Vaccination is effective in contributing to the survival of small children and reducing the infant mortality rates.

- Individual Benefits
  Individuals and families benefit as vaccine reduce morbidity by a reduction in pain, suffering, disability, and mortality from vaccine preventable diseases. Protection through vaccination results in decreasing suffering from disease, and may be hospitalizations and even death.

- Pharmaco-economic benefits
  Societies benefit from ‘herd immunity’ when a high percent of vaccination coverage is achieved and the risks to unvaccinated people decrease. Comprehensive economic assessments of vaccination in both developed and developing nations found vaccines were among the best investments in health. Governments benefit as vaccination compares favorably with other preventive investments with the positive economic impact being in excess of a billion dollars per year.

- Impact of OPPI in Health of Society
  OPPI member companies in India provide healthcare solutions by bringing to the fore prophylactic, therapeutic and diagnostic solutions for various diseases. Vaccines for DPT, Haemophilus Influenza Type b, Hepatitis A and Hepatitis B, Polio, Influenza, Rotavirus, Streptococcus Pneumonia, Cervical Cancer are some examples of vaccines made available by OPPI member companies for protection against diseases in India. Vaccines for Malaria, Tuberculosis, Meningitis, Dengue, Japanese Encephalitis are among some of the other vaccines currently under development.

- Value to Life
  Vaccination has contributed significantly to improving infant survival rates in India over the past decade and also brought down the burden of numerous infectious diseases affecting our society. It has helped the government realize certain important parameters of growth on the human development index. Vaccines are one of the most
important tools in the hands of physicians to prevent several deadly and incurable diseases and will remain so.

(2) **Regulatory Environment**

Vaccine development is a complex exercise involving biological processes and is resource-intensive. Considering these facts and the fact that it operates in an uncertain environment, it is important for a conducive regulatory environment that fosters vaccine development.

- **Indian IND (Investigational New Drug/Vaccine):**
  Though there are well defined regulatory requirements, it involves permissions / recommendations / guidance from various departments under the Ministry of Health (DCGI, DHR-ICMR) and Ministry of Science & Technology (DBT). As a result of all this it takes 2-3 years just to initiate Pre-clinical/ 1st time in human studies which affects the competitiveness of India as compared to other countries.

  The “Single window” concept should be established for vaccines against diseases which are highly endemic in the country to provide the opportunity to meet and discuss the “Regulatory Roadmap” with a single authority which could provide relevant project based recommendations, thus enhancing predictability and readiness to invest from the industry.

- **Registration of a vaccine:**
  The process is well defined but needs further refinement to enhance predictability:

  1) Hesitancy in providing clinical trial permissions especially involving “Pediatric population” even if the study in the same population has already been conducted elsewhere in the world
  2) No strict adherence to timelines after sending to “experts” for opinion
  3) Expertise of “experts” in the field of “vaccine development” should be well established otherwise recommendations may not be aligned to global guidelines.

- **Regulations related to Global Vaccine Trials:**
  Currently there is a significant lack of clarity on requirements, timelines (min 6 months & max 1-2 years) and feasibility of approval for global vaccine trials which makes India uncompetitive and prevents early/timely introduction of vaccines in the country (Average of 4-5 years delay compared to other developed/developing countries). There is a need to have permissions in a mutually acceptable timeframe and in a predictable manner. This is important to shorten the time lag as currently permissions are received in India when other countries have already completed the trials.
• **Requirements if there is change (major or minor) in formulations:**
  CDSCO guidelines define the qualifications of major & minor changes which may require clinical trial or lab based studies. There are instances when EMEA/US FDA uses discretionary power and allows the changes conditionally subject to “post-marketing commitment” in order to maintain supply of vaccines in the market. Similar process of evaluation can be adopted by Indian Regulatory Authorities uniformly.

• **Vaccines concerning diseases involving “National Programs” for e.g. Polio, TB:**
  Licensing of vaccines involving diseases which have National Programs should be treated in a proactive and supportive manner in order to encourage research in these highly endemic diseases. Currently there is no mechanism to expedite the decision making process for such vaccines. There is a need to have a predictable time bound process involving a group of experts (including members from the respective programs).

(3) **Vaccine Policy for Improving Vaccination Coverage**

**Vaccine Policy and introduction of new and existing vaccines**
National Vaccine Policy 2011 is a comprehensive document of guidelines/recommendations which if implemented will have an excellent positive impact on our immunization parameters like infant mortality rate and public health at large. While this may take a few years to initiate various processes and the real benefits of the same will be visible only after around 5-7 years, there is an urgent need to address some key issues in the interim.

**Introduction of new and existing vaccines:**

• **Burden of disease (BOD):** Quite often enormous amount of time is devoted to understand Burden of Disease (BOD) to support important new vaccine introductions primarily because of the lack of good countrywide surveillance/epidemiology data. A few excellent initiatives like IDSP (Integrated Disease Surveillance Project by NCDC) will provide data in a few years time. Meanwhile however “epidemiological/mathematical models” should be used to provide “best estimates” to the decision makers. This will avoid the issue of “Lack of evidence is considered as no evidence”.

• **NTAGI:** NTAGI (National Technical Advisory Group on Immunization) meetings can adopt “administrative model” like WHO-SAGE, in order to have meetings at least 2-4 times in a year, where pre-reads may be circulated well in advance with timely minutes of the meeting. The decisions taken during the meetings should be adequately supported by human and financial resources and tracked with appropriate accountability.

• **Expanded Programme on Immunization and beyond:** While considering new vaccines, appropriate focus is required to address “adolescent and adult vaccines”
through implementation of school vaccination programs and vaccination history during employee recruitment (vaccines against Rubella, Influenza, HPV, Typhoid etc). Currently there are no efforts in this direction apart from EPI vaccines in infants and TT in Pregnancy. The EPI program needs to also evaluate performance and uptake of 1st & 2nd boosters.

- **Decision flow (Scientific opinion and financial decision):** New vaccines are taken into consideration only if felt to be affordable/ economical without defining the criteria of affordability. In the best case scenario, based on the identified disease burden, positive scientific opinion should be provided by NTAGI and then a financial Go/No-Go decision should be taken which may be based on pricing and supply security among other factors. This is important as price is dependent on number of doses, number of years and the level of commitment (GAVI: AMC model).

Vaccine introduction in selected states instead of entire country:
There are vaccines which may be relevant to select states and regions in the country (e.g. Japanese Encephalitis, Meningococcal vaccines now and in future malaria and dengue vaccines). There is a need to develop policy guidelines to decentralize such decision making and encourage states to decide as per the local epidemiology regarding introduction of such new vaccines.

**Policy on improving access of vaccines:**

- Move towards a PPP (Public Private Partnership) model or outsourcing model to immunize and to maintain cold chain equipment (e.g. Telecom policy & “toll” highways)
- Focus on growing middle class as most of the time “immunization services” are accessed by those who have no other alternatives (rush in public hospitals, lack of staff and hence long queues).
- Regular PR activities in favor of “Routine Immunization” is required and campaigns like “Pulse Polio” should be undertaken in appropriate manner in order not to dilute the importance of routine immunization.

(4) **Strengthening Immunization Infrastructure**

- **Need for developing health and health information systems**
Developing well-functioning health systems (including health information) that ensures equitable access to vaccines of good quality, seems to be the solution to the stuck quality of existing full immunization rates. This entails re-engineering of health infrastructure to help increase the capacity of health care workers to make decisions based on accurate information. Scalable and comprehensive health information systems solution would require rolling out solutions vertically down the health system hierarchy, from national to state to district and finally to the community level as well as
horizontally in scope of services and functional areas. Mobile phones can become key enablers for the system and using this technology needs serious consideration in a country with very high penetration of mobile phones.

- **Program management – leveraging existing infrastructure**
  Once it is decided to introduce a vaccine in the population what is needed is sound program management for efficient and effective program implementation. Cold chain being the backbone of immunization services, if a weak link appears anywhere along the chain and the system fails, the risk hardly needs to be stressed. Maintaining this cold chain entails substantial distribution cost and the manufacturer should take responsibility for the same. Strengths of the existing immunization infrastructure can be leveraged if one understands the risk environment around immunization infrastructure: supply side risks, batch or production yield risk, input risk, budget and purchasing power risks, credit risk, price-related risk and regulatory and post-regulatory regime risks. A set of major risks associated with logistics which affects decision making are: non-timely delivery, losses in distribution chain and problems in building complementary inputs (e.g. human resources, accompanying products like testing kits and injection supplies), which may not be available in the quantity or location needed to make use of a vaccine.

- **Distribution & Supply chain management**
  Reducing the cost of uncertainty in vaccine supply can be done in the following ways (Global Health Forecasting Working Group 2007):
  1. Reduce uncertainty and risks by making more information available to decision-makers.
  2. Diversifying risk to reduce its cost or hedge in financial markets.
  3. Allocating remaining risks to stakeholders that can bear them at the least cost.

The most effective supply chains involve integration with program and financial planning, forecasting, production, and procurement processes creating a seamless, continuously adjusting system. Two separate vaccine supply chains exist – one that moves vaccine from supplier to the country and the other which moves vaccines within the country. To effectively link these two, better transportation methods and regional storage hubs are needed to stock vaccine in preparation for emergencies e.g. a pandemic (Ref: Kaufmann, Miller and Cheyne 2011).

(5) **Vaccines to Vaccination**

- **Vaccino-vigilance and need to increase awareness**
  Anecdotal adverse reports affect immunization programs, which are stopped only to restart after elaborate inquiries are held. The long term impact of this is resurgence of the disease e.g. pertussis in Japan, MMR and autism in the U.S. There is a need for experts in vaccine development and vaccine delivery to come forward to increase awareness and voice of vaccines which shall help to counter anecdotal safety
concerns. Improvement in Adverse Events Following Immunization (AEFI) systems would be the first step in addressing safety concerns.

Media attempts to balance coverage by provision of equal opportunity to all viewpoints exacerbates the challenges to public confidence in vaccines by allowing outlier views, and small extremist opinions the same media space as views validated through a rigorous process of peer review by the scientific community (Larson H et al. Lancet 2011; 378: 526–35).

Clear guidelines for disease awareness are needed from regulators. Education of media on the nuances of vaccine development and delivery needs to be taken up on a priority.

- **Innovative data collection**
  Combining data on the number of health districts reporting numbers of children immunized and cases of disease seen or investigated weekly with information on expenditure such as the cost of fully immunizing a child – makes it possible for elected and other decision makers to assess how well the program is using its resources, whether it is reaching all areas and whether it is achieving its goals in terms of value for money.

- **Tax concessions**
  Overhead taxes imposed on vaccines such as excise duty, value added tax (VAT), customs duty could act as a barrier to technology transfer and innovation integration. On the other hand tax concessions /exemptions for the users (on the amount spent on vaccination) on completing vaccination could be an incentive to increase coverage.

- **Improving access**
  Innovative technologies and programming solutions should be utilized to improve access to vaccines in slums and villages with poor power supply. The success of all these would need the coordinated efforts of all stakeholders. Massive investments have taken place over the past decades in strengthening the required infrastructure & building capacities of the Health Care Workers related to vaccine delivery (Evidence-based National Vaccine Policy 2010). Yet, large gaps remain in the planning and execution of the immunization program in many states (rural as well as urban areas), as is evident from the low coverage of primary vaccines under the Universal Immunization Programme (UIP, NRHM 2009). This reduces the effectiveness of vaccines and masks the true demand for vaccines.

  There is an urgent need to look beyond just pediatric vaccination as newer vaccines targeting other age groups such as adolescents and adults, particularly the more susceptible elderly population, are gaining ground scientifically.

  As paramedics play a crucial role in implementation of an immunization program, training of these people needs emphasis and priority.
**Additional vaccines in high coverage states**

It would be helpful to roll out additional vaccines, such as Hib, HepB, rotavirus, and inactivated polio vaccine in preparation for the post-polio eradication scenario in states that have demonstrated high levels of routine immunization. Some steps are already being taken in this direction.

(6) **Innovative Financing**

One of the most effective mechanisms to ensure the sustainability of health interventions is for a country’s self-financing to replace historically fragile external funding sources. The availability of external sources of funds is usually restricted to a particular period of time. National responsibility for paying the bill for vaccines relieves countries of the uncertainty that external financing may not be available when they need it (Andrus, Jauregui, De Oliveira and Ruiz Matus 2011).

Understanding fully well that government will have several financing priorities, we need to come up with innovative financing mechanisms to support the vaccine value chain –

- **Indigenous manufacturing for local market**
  - Government support and subsidies for land acquisition, setup and operating a vaccine manufacturing setup in India
  - Tax breaks for local manufacturing of vaccines
  - Flexible funding from banks and Non-Banking Financial Companies for supporting Good Laboratory / Clinical / Manufacturing practices and ethics. Benefits in the form of lower taxation or other ways of rewarding Good Manufacturing Practices
  - Corporate support for indigenous development of relevant technology platforms

- **Innovative funding mechanisms of R&D and IPR management**
  - Government and private sector collaboration for R&D funding - PPP for funding, intellectual property & portfolio management, and governance
  - Success based part reimbursement of R&D funding by public and private stakeholders
  - Progress based insurance cover on successive R&D phase funding
  - Better management of IPR to encourage innovation and access
  - Collective vaccines fund to support development of vaccines for emergency or epidemic situations
  - Funding for scientists and investigators working in vaccines development lasting for at least 5 years
  - Rewards for innovative discoveries

- **Payor mechanisms**
  - Insurance coverage of vaccine expenses
  - Tax exemptions on vaccine related expenses
- Necessary budget reforms to earmark a larger proportion of government spend for R&D and manufacturing of vaccines. Reset budgets based on progress and performance reviews
- India specific AMC through which Government can commit to a minimum price to be paid per person immunized up to a certain fixed number of individuals immunized (Berndt, Glennerster, Kremer, Lee, Levine, Weizsacker and Williams 2007)
- Government to negotiate a low price for public introduction of a vaccine with the manufacturer, with the proviso that reliable long term contracts for vaccine supplies would be awarded

The implementation of the above innovative financing mechanisms will provide a significant boost to vaccines and immunization in the country. OPPI shall ensure continued support for these important issues which are essential to achieving our country’s health goals.

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