National Seminar on New Vaccines for All: Why, Which, When?

October 20-21, 2016

Organised by:

Jan Swasthya Sahyog (JSS), Sama Resource Group for Women and Health,

Forum for Medical Ethics Society (FMES) and National Medical Journal of India (NMJI)

Venue: National Institute for Health and Family Welfare (NIHFW)

National Seminar on New Vaccines for All: Why, Which, When?

The National Seminar on 'New Vaccines For All: Why, Which, When?' was held on October 20-21, 2016 at the National Documentation Centre Conference Hall, National Institute of Health and Family Welfare (NIHFW), New Delhi.

Dr. Yogesh Jain, Ms. Sarojini N and Dr. Amar Jesani, members of the co-organising committee of the seminar are also the members of the Mission Steering Group (MSG) of the National Health Mission (NHM). A range of issues on new vaccines and combination vaccines had emerged during the MSG meetings and it was felt that such a seminar would be an opportune platform for a robust deliberation on their varied aspects.

Other recent developments with regard to vaccines also prompted the conceptualisation of the seminar. Firstly, hepatitis B vaccine had been included in the Universal Immunisation Programme (UIP) a few years ago, which initially included six vaccines. Secondly, the pentavalent, a combination vaccine is being introduced in a phased manner in the UIP. Thirdly, a slew of new vaccines against rotavirus, rubella, human papilloma virus (HPV), pneumococci and the injectable inactivated polio vaccine were under consideration.

These developments have led to the question - Which new vaccines should be added to the national immunisation programme? Introduction of any new vaccines must be assessed critically for human use in terms of their suitability, safety, protective efficacy and affordability before adopting them into UIP. Moreover, whether the public health system has the organisational capacity to deliver and monitor additional vaccines at an appropriate time, without affecting the coverage of existing vaccines or other health services should be evaluated in accordance with the National Vaccine Policy. Further, in the context of some of the new vaccines, the decision of introduction must also consider other existing public health measures for disease control towards ensuring that the vaccines do not shift focus away from the latter.

The national seminar sought to facilitate a dialogue on 'New Vaccines' in the true spirit of public health, and of a high scientific quality towards building perspectives and consensus, where possible, on these issues. It was successful in mobilising participation of representatives from the Ministry of Health and Family Welfare (MOHFW), Indian Council of Medical Research (ICMR), World Health Organisation (WHO), Institute of Economic Growth, public health institutions, civil society organisations, academic institutions, medical colleges hospitals and research institutions, etc.

The key outcomes from the seminar deliberations were expected to contribute to future policy level recommendations. These will also be further discussed at the International Conference on Vaccines to be organised by the Ministry of Health and Family Welfare (MoHFW) in 2017.

The first day of the seminar comprised three sessions. These included a session on the present status of children's health and vaccination. The second session was on prioritisation of interventions for disease prevention, followed by the session on inclusion of new vaccines in the UIP. The sessions on the second day included deliberations on risk assessment and safety; on cost effectiveness and financial issues; on ethics, laws and regulations; and, on the health system's preparedness.

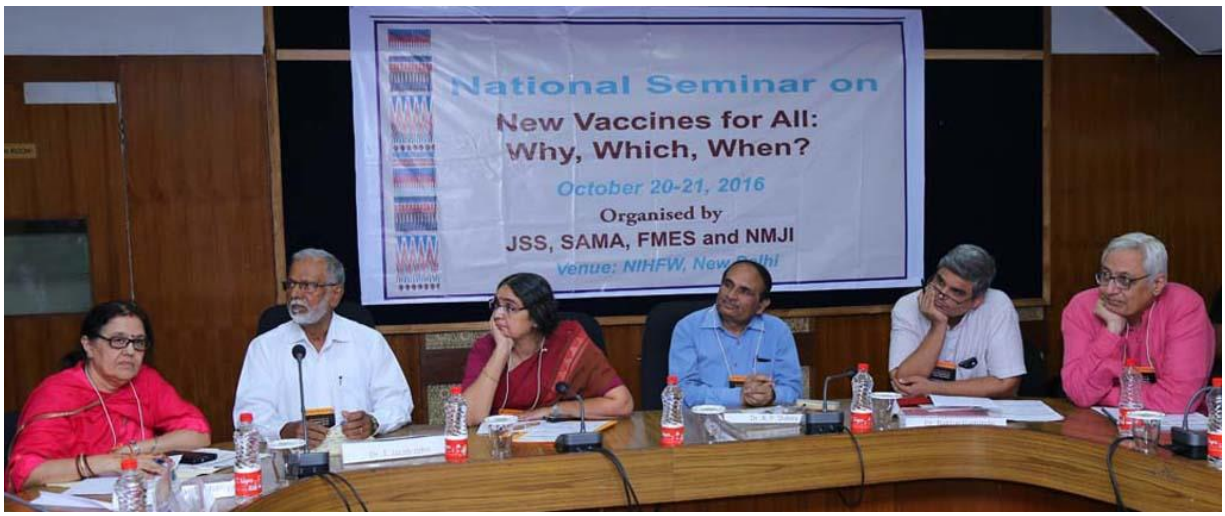
Highlights from the Seminar Sessions

Session I: Present Status of Children's Health and Vaccination

The presentations in this session were made by Dr. T. Jacob John (CMC Vellore), Dr. A. P. Dubey (MAMC) and Dr. Rakhal Gaitonde (IIT Madras).

- There is a need to critically look at the immunisation programme as more than a vaccine delivery platform. It was argued that we need a health system based on disease control strategy rather than on a vaccine delivery programme. There is a need to create a bridge between the individuals and the community, and acknowledge that healthcare (for the individual) and public health (for the community) must go hand-in-hand.
- Vaccine effectiveness and the National Immunisation Programme must aim to concentrate on the causes of the diseases that they seek to address. Further, there are two modalities – healthcare restoration which must be based on the principle of 'fairness' and the public health system that must addresses the 'equity' aspect. The national programmes in their current form do not have a goal of disease control. It lacks a good surveillance system to measure the disease control research. The government needs to allocate the requisite resources towards a robust surveillance system. There is a dearth of studies that measure disease control for childhood tuberculosis, hepatitis B Virus (HBV), Japanese Encephalitis (JE).
- It is important to stress on having a public health department in the country. The need of the hour is to accelerate the groundwork on the impact of immunisation and not just impact on diseases, in order to be able to add more new vaccines in the UIP.

- In terms of universal coverage, India lags behind in the task of achieving universal coverage of one year old children immunized against measles, according to the Coverage Evaluation Survey (CES) 2009 by UNICEF and Government of India. The CES estimated the proportion of one year old children immunized against measles was 74% in 2009. Although, this shows that there is substantial improvement in the coverage from 42% in 1992-93, yet at this rate of improvement, India was likely to achieve about 89% coverage by 2015 and thus fall short of universal coverage. There is also a rural-urban gap in this coverage – 72% in rural areas compared to 78% in urban areas. Moreover, the coverage of measles immunisation was nominally high in case of male children (74.8%) than female children (73.2%).
- While it is also important to acknowledge that certain goals in terms of immunisation coverage, like reducing infant mortality has been achieved, it is equally imperative to do an equity analysis of these targets. Need to look beyond the numerical data and do a critical analysis to include the most vulnerable who often remain excluded from our analysis. There is also a need to develop an understanding on what can be the realistic benefits from vaccination. National Policy on Vaccines (2011) focuses on vaccines alone instead of focusing on communicable disease control within which vaccines should be placed.
- There are concerns over shifting vaccine industry to the private sector while slashing the budget for the public healthcare system. It is important to underscore that the private sector has a profit motive, whereas the prerogative of public sector is to uphold the human rights concerning health of the people. The current policy does not talk about the social determinants of health, which it should.
- While it is greatly known today that access, coverage and the way human bodies produce antibodies and respond to vaccines vary according to one's nutritional status and other social determinants.



Session II: Prioritisation of Interventions for Disease Prevention

Prof. Vinod Paul (AIIMS), and Dr. Rakesh Lodha (AIIMS), Dr. Madhavi Y (NISTADS) spoke on issues concerning interventions and priorities with regard to vaccines.

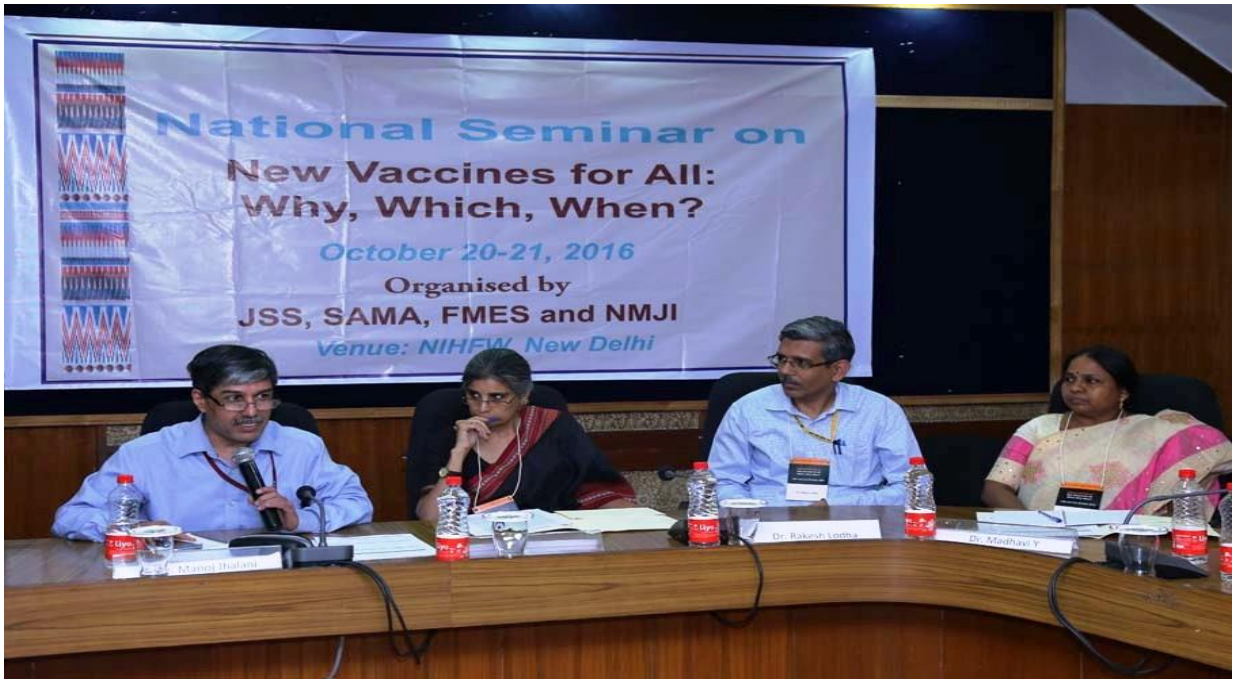
- The criteria like potential impact, safety, comparison with other approaches to avert morbidity/mortality, cost versus gains, and equity lens with regard to its outreach to the

poor, should be considered while prioritizing on including new vaccines. The importance of assessing the impact of the vaccine in terms of prevention of morbidity and mortality was raised.

- In cases where burden of disease data is not available, data from neighbouring areas can be extrapolated to understand the effectiveness of the vaccine. Moreover, the macro level questions regarding the health system, like, the availability of funds, human resource, delivery systems like cold chain, how it will be phased out and how to address the adverse events following immunisation (AEFI), are to be considered as well.
- The social determinants of health are important to understand holistic picture of disease control, as vaccine is a part of this process. Health is not limited to healthcare provision only; rather it is an outcome of individuals' response to society, community, social position and environmental condition they live in. Healthcare contributes between 15-40 percent of factors driving health and health behaviour.
- Inequity invariably impacts health as the poor have less access to resources and higher exposure to risk factors. The global disability adjusted life years data (DALYs) shows that contributing risk factors for poor health outcomes are lack of nutrition, hygiene and occupational risk among others. In India too, changes in the multi-dimensional poverty index show increasing rates of morbidity and mortality due to air pollution and child under-nutrition among other factors.
- The example of diarrhea aetiology, which indicates how the process of treatment has to be a combination of vaccine introduction and changes in environmental and social situations like hygiene, hand washing and better nutrition. For introduction of vaccine, annual investment may be small but the same has to be sustained. Comparing the WASH initiative versus vaccine introduction for diarrhea, he stated that the decision making should take into consideration whether there is need for integration across systems, first to ensure better hygiene and sanitation which may raise vaccine efficacy.
- Today the mode of vertical programs, lack of integration across ministries like MoHFW has no control over water supply, leads to a loss of the holistic approach to ensure better health outcomes through a more consolidated approach. Though we cannot wait for all social determinants of health to improve, some health interventions may work better if they do. So there is need to introspect why a pro-vaccine debate is heard more than the social determinants argument. For example, why is safe water still a problem in India that needs to be critically questioned.
- The role of vaccines instead of being seen as opposed, it can be seen as supportive and there is a question for us to decide about; with low or high resources, whether the intervention and disease control should be done sequentially.
- It was suggested that non-vaccine interventions and vaccine interventions should be done together but would only be possible with larger budgets.
- The following presentation on balancing priorities in vaccine policy discussed that vaccines should be safe, affordable and accessible. They should work against the local pathogen specific to certain population or geographical area. For this, one needs to know what the real burden of disease is. Based on this, the decision should be taken on which vaccines are to be introduced in the UIP to address uniform disease burden and which ones should be introduced selectively only for local endemic diseases.
- In addition to ensuring affordability, there should be promotion of local production of vaccines and the bulk production at Public Sector Units (PSUs). The logic guiding the

introduction of vaccines should be rooted within the disease burden. The logic of introducing combination vaccines was questioned; is it based on business logic or does it stem from medical logic i.e., response to the burden of disease.

- Grave concern exists about the scenario in India today where there is a proliferation of new vaccines and orphanisation of old vaccines, simultaneously. There is a withdrawal of the public sector from vaccine production in the post TRIPS period so the government has to procure vaccines at a high price from the private sector, distorting the supply.
- This impacts access and affordability of vaccines. It was conclusively submitted that there is a demand supply gap in the UIP currently, which can be mitigated by promotion of public sector production. A strong case was made during the discussions for ensuring facilities for vaccine production before we think of new vaccines.
- Another issue that displayed a growing concern is that of combination vaccines where the safety of the combination vaccines is not clearly determined.



Session III: Inclusion of new vaccine in the UIP: How effective are new vaccines?

Dr. Vineeta Bal (NII) presented on effectiveness and efficacy of vaccines with a particular focus on Human Papilloma Virus (HPV) vaccine and the Rotavirus vaccine.

- In the context of the HPV vaccine, two important points to be considered: prevention of the disease and protective response generated by a vaccine. Effectiveness of vaccines is determined by their ability to provide protection from a disease, that is, by generating a protective immune response. This is different from efficacy- which determines the vaccine response in a clinical trial situation, which is in a relatively more controlled environment.
- Clinical Trials efficacy (identified in blood levels) comes down drastically in the field. So there is a difference in the vaccine efficacy in a clinical trial and during actual

administration. Surrogate marker of protection of the vaccine is tested during clinical trial.

- Vaccine provides protection from disease, not from normal infection, which is prevalent everywhere. Immune system responds to infection, which lasts for different vaccines with different time durations. Therefore, vaccines can provide different duration of protection- some may require boosters after a period.
- There are multiple HPV viruses. The vaccine can mount an immune response post sexual activity when HPV is contracted – but it cannot provide protection from all strains of the virus. HPV - Strain A works after sometime; Strain B vaccine will work for both. If vaccine is given at one point and another virus comes in the way, the individual will generate an immune response to it. So there may be cross protection as well.
- Vaccines should be tailor made. There is no single solution for the types of vaccine we take- all five components of the Pentavalent vaccine will generate separate response in trial conditions so together they may have a protective factor but this may differ according to situations. However, it is not the same for Polio IPV and OPV.

Session IV: Inclusion of new vaccine in the UIP: Risk assessment and safety of vaccine

Dr. S. K. Mittal (Max Hospital, ex MAMC), Dr. Jacob Puliyel (St Stephen's Hospital), and Dr. L. Machado (WHO) presented on safety profile of vaccines, adverse events following immunisation (AEFI), and on inclusion of new vaccines in UIP.

- The literature on vaccines is mostly positive, and does not focus much on safety and efficacy issues. Any negative aspects associated with vaccines are relegated to the margins of the discourse.
- Vaccines can have side effects, but it is difficult to establish a causal relation between administration and vaccine reaction. Post vaccine surveillance is very important but large companies are unwilling to set up such processes; only through reports or stray reports do we get any idea of what is happening.
- The rotavirus vaccine was discussed; extensive epidemiological data exists that diarrhoea is a major cause of death. However, rotavirus vaccine is not a solution for diarrhoea. The serotypes keep changing. The Rotavirus vaccine thus has limited impact on infant mortality rate (IMR).Even with 100 percent coverage, prevention is only eight percent. Studies exist that show that indigenous Rotavirus Vaccine has 60 percent efficacy; however, some research papers on it were sponsored by Glaxo SmithKline (GSK), the pharmaceutical manufacturer. In one paper, 26 of 27 authors declared conflict of interest as they had connections with GSK.
- Robust and mandatory norms and mechanisms for reporting and investigating, vaccine injury prevention and compensation should be put in place.
- The case that was highlighted during the discussions was of three Pentavalent deaths in Sri Lanka, following which the WHO deleted the criteria of "probable" and "possible" and declared that the deaths were not related to the vaccines from the Council for International Organisations of Medical Sciences (CIOMS)/WHO guidelines.
- Concerns were raised regarding the guidelines in which a case of AEFI was turned into non-AEFI, even though it shows possible or probable link for causality. The former "probability" scale to assess causality for investigating an AEFI included six criteria – "certain", "possible", "probable", "unlikely", "unrelated", and "unclassifiable".
- This scale has been revised to strike off "possible" and "probable", raising concerns over flaws in the investigation of AEFI. The guidelines mentions that an event can be called an AEFI only if a similar event is proven in previous epidemiological studies. The new algorithm devised under CIOMS/WHO guidelines and the AEFI, which was not noticed in epidemiological studies previously, will be deleted, such that there will be no record of them and thus they cannot be investigated. The challenge is to remove the obfuscation surrounding the investigation of AEFI.
- There have been deaths and serious adverse events (SAEs) following the Pentavalent vaccine. The evidence is with the government, but is not being made public. The paediatricians are using this vaccine, as they believe they are helping children. But, the AEFI are not taken seriously.
- The representative from WHO, while speaking on AEFI causality assessment protocol shared existing challenges in following up on adverse event. There are challenges in collecting data from the field and there is need to understand the ground realities. Every block primary health centre (PHC) has a reporting mechanism in place for AEFI. The WHO

is trying to help medical officers to collect the information in as detailed a manner as possible. Causality assessment is done at the state level, not at the district level.

- 670 out of 683 odd districts have district AEFI committees. Some limitations exist in both government and private hospitals, such as staffing, documentation gaps, etc., in terms of implementation of the protocol.
- It is a now a mechanical process, with an eligibility criteria to determine if the AEFI satisfies the minimum criteria for causality assessment. The checklist systematically review the available information and algorithms are use to obtain a trend in causality.
- Unfortunately, where there is prior evidence the approval if the vaccine is fast tracked, and waiver of phase III clinical trials maybe given by the Drug Controller General of India (DCGI). However, careful assessment needs to be done, prior to granting waiver. The AEFI is not just a statistical number, but needs to be taken seriously, and the definition needs to change.

Session V: Ethics and Regulations

Dr. S. Srinivasan (LOCOST Therapeutics/AIDAN), Ms. Sarojini N (MSG/Sama), and Advocate Veena Johari (Courtyard Attorneys) raised critical issues of data transparency, regulatory neglects, and conflict of interest vis-à-vis clinical research, rights of the people and the process of immunisation.

- The importance of data transparency and public availability of anonymised raw data was unequivocally raised during the discussions. Patients are the real beneficiary of data sharing.
- Access to data concerning clinical research is a matter of right for the people linked their right to health. Thus, it should not be dependent upon the goodwill of the sponsors. Access to data is critical as it facilitates the confirmation of results, and will prohibit selective publishing of findings based on the data. However in practice, data is often not

shared even if a request to procure the data is routed as a right to information (RTI) application.

- Patients are the real beneficiary of data sharing. Clinical trial data should be made available and there should be openness and transparency in sharing the clinical trial data.

This session also focussed on compensation systems for vaccine related adverse events, ranging from minor harm to major injuries, that can result in temporary disability or a disastrous injury leading to permanent disability or even death. These compensation systems vary across countries and are being debated globally.

- The elements of compensation in different countries include: unreimbursed medical costs, disability pension, non-economic loss, funeral costs, future care cost, lost wages and death benefits. An obligation to compensate for injuries is grounded in a number of ethical principles of justice, fairness and human rights. The source of funds for the compensation is also a matter of debate - whether it should be the government treasuries or manufacturers' levy paid by the pharmaceutical companies. For example, in Taiwan and USA, a vaccine tax becomes the corpus for paying compensation for vaccine related injury.
- The discussion included how vaccine injuries can be assessed and where should the decision making in this regard rest. Whether the data /reports from AEFI can be used to assess the injury for the purpose of compensation, moving beyond the classification of AEFI is also necessary.
- To draw upon the case of clinical trials where compensation provision exists, there are arbitration processes, which often lead to a conflict of interest that need to be resolved. Such inconsistencies should be guarded against in a compensation system for vaccines.
- It is important to deliberate whether all physical, emotional, and psychological injuries should receive compensation (including economic loss). Clarity is also needed on deciding the form (e.g., whether only medical care or monetary compensation are appropriate for long term injuries) and quantum of compensation even if a law is put in place for disbursement of compensation.
- Moreover, focus should not be just on product but also the process of administration in case of vaccines. Currently, the process of redressal is primarily through legal action by those affected; necessitates recognition of injury following vaccination and compensation policy. This can be pursued at the policy level.
- Currently, we do not have any official vaccine compensation scheme or programme in the country. Complainants have no other option but to approach the legal system using tort laws. The litigation process is lengthy and very expensive. Establishing causality and fault is burdensome for the complainant. Case law shows that long time intervals are common in getting a court order, ranging from 11 to 32 years, with no certainty of getting a favourable decision from the courts.

The following pertinent questions were raised while discussing compensation:

- Should all physical, emotional, and psychological injuries receive compensation (including economic loss)?
- Is medical care all that is required? Should monetary compensation for other losses be provided as well for long- term injury?
- Who should be paying the compensation; should it be the pharmaceutical companies or the government?
- What *should be the mechanism of surveillance?*

It was conclusively agreed that recognition for compensation in instances of vaccine related harm or injury is urgently required in both public and private sectors.

The discussion on compensation was followed by a focus on informed consent from human rights perspective, which includes right to life-privacy, confidentiality and autonomy. The speaker argued that it is the State's legal duty to perform an assessment of health needs, including the need of vaccines. It is to be complemented by acknowledging the rights of the people.

- Any public health measure has to be within the boundary of the Constitution. Respecting rights of people empowers them and helps in achievement of public health goals of curbing the spread of disease.
- Duty of the State is to provide honest and complete information ina simple manner in a language that can be understood. The consent should where appropriate, be expressed and may be withdrawn at anytime for any reason without disadvantage or prejudice
- Informed consent depends on access to information. We are often vaccinating the most vulnerable population without even informing them of the risks. It is essential to make such programmes participatory. All systemic problems might be better resolved if the process involves people's participation. The discussion on informed consent generated a lot of exchange of views and the format of seeking consent is still open to discussion.

Session VI: Inclusion of new vaccine in the UIP: Cost effectiveness and Financial issues

Prof. V.R. Muraleedharan (IIT Madras), Dr. Rakhal Gaitonde (IIT Madras), Dr. Ravi Duggal (International Budget Partnership) and Prof. Indrani Gupta (Institute of Economic Growth) shared their expert insights concerning this topic.

- The purpose of economic evaluation helps to select more efficient options (with a good cost/effect relationship) and could help in the distribution of health resources in a more just and balanced manner. It contributes to the rational use of medicines/interventions by incorporating cost to questions on safety, efficacy and quality of different medical therapies/interventions, and to the search for a better relationship between costs and results. It also focuses upon the costs and benefits of drug, therapy/programmes/ Interventions, limited resources setting, maximum health impact from a given budget and cost-effective intervention.
- The economic evaluation of the costs and health effects of vaccines also depends on resources. Health resources should be allocated across interventions and population groups to generate the highest possible overall level of population health, to improve efficiency. Which costs and outcomes are considered relevant and should therefore be included in the analysis?
- The costing system needs to be strengthened and take into consideration all type of costs. The non-availability of good baseline information or data remains to be challenge. There are issues with regard to access wherein it is seen that UIP coverage is about 60 percent and there is wide variation across states. It makes a strong case to challenge only one set of cost effective analysis (CEA). It should be done at the state level if not at the district level.
- Even though the complexities of making cost effectiveness studies are known, it remains a challenging task to make evidence based decisions without a good public health system, without disease prevention system within it and without other systems in place, which include ways to calculate cost and effectiveness.

- Costs of new vaccines are very high. About Rs.9 to Rs.11 per capita is spent on vaccines in each State. About 50-60% on the vaccines and the remaining on other things like injections, refrigerators, etc. But, with the newer vaccines, almost Rs.35 per capita is

being spent just for the vaccine and the additional things that are required to conduct the vaccination programme increases the vaccine cost per capita up to Rs.75/- .

The cost analysis of vaccines needs to be improved. Vaccines selected or analysed should require the costs to be considered.

The discussions raised concerns about how we do not have reliable data to assess cost effectiveness, which presents a challenge of lack of evidence to decide upon the inclusion of specific vaccines. Studies show that countries consider efficacy, safety and effectiveness very rarely. The disease burden is a key factor while deciding on vaccines. Programmatic considerations with a weak health system should be a major concern, but it is usually not considered.

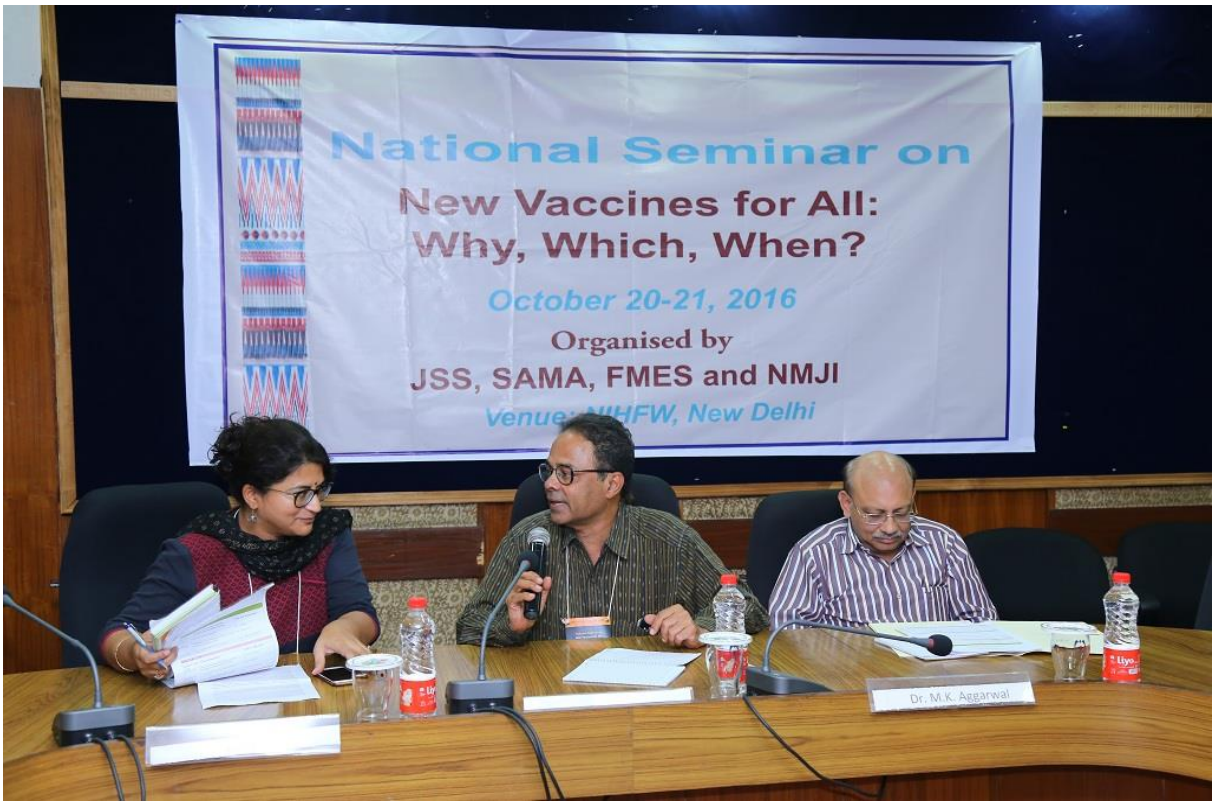
- There is also a dearth of literature and studies on the community acceptability of vaccines in the Indian context. Accessibility, ethics and equity are infrequently considered and system costs are rarely mentioned. Vaccine price is seen to be an important variable in deciding on including a new vaccine in a national programme.

Session VII: Inclusion of New Vaccines in the UIP: Health System Preparedness

Dr. Jyoti Joshi (ITSU,PHFI) and Dr. M.K. Aggarwal (MoHFW) presented on the robustness of the public health surveillance to monitor AEFIs and on health system preparedness for introducing new vaccines.

- Any new vaccine introduction in India follows a systematic procedure and is an informed evidence based policy decision. It is based upon a comprehensive review of existing evidences, programmatic challenges and system preparedness. A multi-level consultative process is followed with key stakeholders.
- In the pre-introduction stage of a new vaccine, capacity building is undertaken for various health cadres towards building awareness and refreshing their knowledge about the entire immunisation programme. Detailed micro-plans are prepared and updated regularly providing details of session date, site, vaccinator name, etc. which are revisited and updated with the introduction of every new vaccine.
- Before introduction of any new vaccine, a complete communication plan is developed to ensure that the message of new vaccine as well as other vaccines under UIP reaches the beneficiaries.
- Every new vaccine introduction is followed by a Post Introduction Evaluation (PIE) after 6-8 months of rollout. PIE is based on a global tool used to assess the preparedness, strengths and weakness of new vaccine introduction. PIE reports are publicly available and supports govt. in further streamlining efforts toward a well prepared system.
- Public health surveillance is the ongoing systematic collection, analysis, and interpretation of data, closely integrated with the timely dissemination of these data to those responsible for preventing and controlling disease and injury. The purpose of surveillance is to empower decision makers to manage more effectively by providing timely, useful evidence. Like for drugs, vaccines also require a surveillance system that can capture any untoward cases.

- There are at least three general types of surveillance systems that can be applied to monitoring and management of AEFI and vaccine safety: Passive Surveillance which requires the population or healthcare workers (HCW) report any condition that they believe could be associated or related to a vaccine event; Stimulated Passive surveillance similar to passive surveillance but in which the system encourages the reporting of events in the community or at the HCW level; and Active Surveillance which involves systematic search for defined AEFIs in specific populations to try to determine the scope and the true incidence of the events.
- An AEFI is any untoward medical occurrence which follows immunisation and which does not necessarily have a causal relationship with the usage of the vaccine. The adverse event may be any unfavorable or unintended sign, abnormal laboratory finding, symptom or disease. AEFI may not be causal but there is always a temporal relation. Through a robust surveillance net it is possible to capture AEFI at hospitals, clinics, community (through health care workers) in order to examine whether it has a consistent causal relationship.
- The Universal Immunisation Programme (UIP), the Pharmacovigilance Programme of India and the Central Drugs Standard Control Organisation (CDSCO) are important data sources for monitoring vaccine safety.
- Need to create enabling environment for AEFI reporting involving treating clinicians, formal and non formal health practitioners. State and district level capacity to be improved to conduct timely investigation and assessment. Awareness of the concept of AEFIs among clinicians and reporting to public health program needs to be strengthened.



Recommendations

1. The Government of India should adopt a paradigm shift for Universal Immunisation Programme (UIP), from immunisation delivery to disease control with adequate public health infrastructure.
2. Introduction of vaccines must be complemented with addressing the Social Determinants of Health (SDH) that affect and determine the situations of healthcare with equal commitment, particularly for the most vulnerable groups of people in our society.
3. Wherever occurring significant doubts about effectiveness and safety profiles of the new vaccines must be addressed rigorously.
4. Compensation should be paid for all forms of vaccine related injuries and harms.
5. Data sharing should be ensured for independent verification forthwith, in the larger interest of public health.
6. All the clinical trial data and the adverse events that are serious in nature should be made available, analysed by experts, and placed in the public domain.
7. The Government of India should formulate guidelines for Adverse Event Following Immunisation (AEFI) investigation drawing upon the existing global frameworks
8. Cost Effectiveness Analysis (CEA) Studies should be conducted before any new vaccines are considered.
9. Public sector production of vaccines should be prioritised instead of purchasing from private companies whether Indian or foreign Multinational Companies (MNCs).
10. Rights to privacy, confidentiality, information and autonomy of individual recipients of vaccines must be upheld and protected.

Annexures

Annexure 1: Background Note of the Seminar

New Vaccines for All: Why, Which, When?

Over the last few years, to the initial six vaccines against tuberculosis, diphtheria, whooping cough, tetanus, poliomyelitis and measles, Hepatitis B vaccine has been included in the Universal Immunisation Programme (UIP). A combination vaccine against diphtheria, whooping cough, tetanus, poliomyelitis and hepatitis B, the pentavalent vaccine, is being considered for inclusion in the UIP, but not without attendant doubts and questions. Further, a slew of new vaccines are competing to get into the national schedule. These include the vaccines against rotavirus, rubella and Human Papilloma Virus, and injectable inactivated polio vaccine. These developments have led to the following question - Which vaccines should be added to the national immunisation schedule, so that they are offered to all children in the country? The answer to this question should be based on evidence that a particular vaccine is, compared with other interventions, not only more effective against an infectious disease of public health relevance but is also safe and cost effective on the ground and is affordable for the country. Further, the public health system should have the organisational capacity to deliver the new vaccines at appropriate times, without a negative impact on the coverage of the previously used vaccines, or on any other services offered by itand it should be able to monitor the effectiveness and safety of the vaccines. Accordingly, the National Vaccine Policy recommends a detailed evaluation of these factors before a decision to include a new vaccine is taken.

How do new vaccines find their way into the national schedule? Once a vaccine has gone through the mandatory stages of testing, professionals, public health experts and possibly vaccine manufacturers lobby and submit proposals for inclusion of a candidate vaccine into the national schedule for approval by a National Technical Advisory Group on Vaccines (NTAGI), a body that includes technical experts chosen by the Ministry of Health. This is a closed group, which deliberates and finally comes out with a recommendation based on majority voting that is then put up to the Ministry of Health for consideration of final administrative decision making and for making budgetary allocation.

Vaccines are unique given that they are the only medicines given on a mass scale to healthy people. Hence not only are they expected to adequately prevent the illnesses for which they are meant, they are not acceptable by the community in case of any major adverse events such as hospitalisation, death or disability. That majority of vaccines are given to children in their first months of life, which is a vulnerable period as it is, make safety concerns doubly important. Further, there is a greater need for well-functioning health systems to run universal and effective vaccine delivery and monitoring systems for a preventive programme than is needed for, say, a malaria treatment programme.

The situation is further complicated by another set of processes that operates for some vaccines. There are a few vaccines that have variable levels of effectiveness in preventing potentially life threatening infections such as pneumococcal infections, typhoid or there are those vaccines which protect against those illnesses that may result generally in milder and sometimes troublesome illness such as chickenpox, hepatitis A and mumps. Then there are vaccines like those against Human Papilloma Virus (HPV) which variably protect against cancer of cervix and some other cancers. All these vaccines are presently far too expensive for being considered for universal use. They are being recommended by several medical professional bodies to an 'affording population'. Some people would question: in case of some of these new vaccines the people who can afford new vaccines are least likely to acquire these infections against which these vaccines provide protection. So why go for it. Others would argue that since vaccines are a biological drug, and is no different from any other technology that the people who can afford it should go for it, and that physicians should prescribe it. The fact that all vaccines are prescription drugs and are not consumer products open to personal choice and affordability only makes matters more complicated.

We cannot deny that vaccines also mean big business, if they are used in large populations, as would happen for a universally used vaccine and even if the unit cost is low. Pharmaceutical companies claim that they invest huge amount of money in producing new vaccines and, therefore, it is legitimate to accrue huge profit from their sale. It is another matter that they spend more on marketing than on research. Strengthened regulatory mechanisms and checks and balances must be in place towards objective recommendations and so that professional bodies like NTAGI are able to remain objective and take decisions based on scientific evidence.

Given this background, as it stands today, there is confusion and paucity of correct information, lack of trust and breakdown of dialogue among all stakeholders on the question 'whether a vaccine deserves to be included in the national Immunisation schedule.' The stakeholders include- medical Scientists and vaccine experts, health administrators, doctors, parents and the lay public. Even now, NTAGI or for that matter any other technical body, has not been able to convince the people about the safety of some of the new vaccines such as pentavalent and both safety and effectiveness of rotavirus vaccine by coming out with well researched and referenced guidelines. Changing the methodology of investigating adverse events following immunisation recently, and inadequately investigated AEFI without adequate transparency, furthers the sense of distrust between those vaccine enthusiasts and those who question such events and are branded as 'anti vaccine lobbyists', NTAGI should place all evidences regarding safety and efficacy of a new vaccine in the public domain so that it could be scrutinised by independent experts. For prevention of many of these infections that these vaccines prevent, there are other preventive measures such as improving water quality and sanitation practices or improving health care services or food availability, where data show that it is more cost effective to do the former.

The Centre has drastically slashed the health budget while it has decided to spend a large amount of money on inclusion of some of the new vaccines in the National Immunisation Schedule. Even if we say that we should go for both vaccines and improving social determinants of these illnesses, arguing for vaccine first and these measures later tends to unburden the state of its responsibility to provide the latter.

The need of the hour is to have a dialogue on "*New vaccines'* in the true spirit of public health and should be of high scientific quality that moves towards building a consensus as well as a perspective on this issue.

The dialogue will be divided over two days - the first day will include three sessions with the first discussing vaccine research in India, Government policy on new vaccines. The second session is on *Prioritisation of interventions for disease prevention,* followed by the third session on *Inclusion of new vaccine in the UIP: How effective are new vaccines?*

Day two will include deliberations on risk assessment and safety; cost effectiveness and financial issues; on ethics, laws and regulations, and on the health system's preparedness.

The sessions would include discussions on the questions of: At what level of cost effectiveness should one advise a vaccine as a public health tool for the governments to take cognisance of? What incidence of side effects is too much for a vaccine to be advised as a preventive health technology? What is an acceptable death rate in a vaccination programme? Would this 'acceptable level' be the same for all vaccines or would it depend upon the incidence and consequence of the infectious disease on the one hand and the incidence and severity of side-effects of the vaccine on the other? How is an investigation into an AEFI done and then documented and publicised? And then compensated for? When there is more than one tool besides a vaccine to prevent a disease, how do you weigh which one is more important? Is it really important to measure it[1]?

The most transparent way to handle a new vaccine introduction should be a technical report accompanying the launch, which lays out the pros and cons and takes a clear stand on what were the reasons why the vote went in favour of a new vaccine. Is this something that NTAGI should do?

Tempered by principles of science and equity and justice concerns, the dialogue is expected to deliberate on: Which new vaccines do we think should be included in the National Immunisation Programme of India?

Jan Swasthya Sahyog (JSS) Bilaspur, Sama Resource Group for Women and Health, Delhi, National Medical Journal of India (NMJI) and The Forum for Medical Ethics Society (FMES) Mumbai, would be co- organising this Seminar.

Concept note by:

Dr. Yogesh Jain (JSS), Ms. Sarojini N (Sama) and Dr. Amar Jesani (FMES)-Members of Mission Steering Group of National Health Mission (NHM)

[1]Some people would argue that this relative cost argument is not very real, because there is greater possibility of a child receiving a vaccine than a sanitary latrine, given the implementation challenges for the latter.

Annexure 2: Seminar Schedule

Day One: 20th October, 2016		
Time	**Theme/ Session**	**Speakers & Chairs**
09.00-9.30	Registration	
09.30-10.00	Welcome, Objectives of the Seminar and Participant Self-Introductions Welcome	Organisers Dr J K Das, Director, NIHFW
10.00-10.15	**Key Words: Mr C.K Mishra, Secretary Health, MOHFW - TBC**	
10.15-10.30	**Tea**	
Session 1 **10.30-12.45**	**Present Status Of Children's Health and Vaccination**	**Chair: Dr. Soumya Swaminathan (DG, ICMR) - TBC**
10.30-10.45	Child Health in India: Current Status and Goals	Dr. A P Dubey
10.45-11.00	Journey of UIP in India	Dr. Chandrakant Lahariya - TBC
11.00-11.15	Burden of Disease & Effectiveness of Vaccines in the UIP	Dr. T Jacob John
11.15-11.30	Prioritisation of New Vaccines in Government Policy	Dr. Rakhal Gaitonde
11.30-12.45	Discussion	
12.45-13.45	**Lunch**	
Session 2 **13.30-15.15**	**Prioritisation of interventions for disease prevention**	**Chair: Mr. Manoj Jhalani (JS, MOHFW) and Dr. Vandana Prasad**
13.45-14.00	Role of vaccine in disease prevention	Prof. Vinod Paul
14.00-14.15	Effectiveness and benefits of investment to improve determinants of health	Dr. Rakesh Lodha
14.15-14.30	Balancing Priorities in Policy Making	Dr. Madhavi Y
14.30-15.15	Discussion	

15.15-15.30	**Tea**	
Session 3 **15.30-17.00**	**Inclusion of new vaccine in the UIP:** **How effective are new vaccines?**	**Chair: Dr. Anant Phadke**
15.30-15.45	Effectiveness of vaccines: Rota Virus and Pneumococcal vaccines	Dr. Gagandeep Kang
15.45-16.00	Effectiveness of vaccines: HPV and Other Vaccines	Dr. Vineeta Bal
16.00-17.30	Discussion	
Day Two: 21st October 2016		
Session 4 **09.30-10.45**	**Inclusion of New Vaccine in the UPI:** **Risk Assessment and safety of vaccine**	**Chair: Prof. Imrana Qadeer**
09.30-09.45	How Safe are New Vaccines?	Dr. S K Mittal
09.45-10.00	Challenges and Investigations of Adverse Events Following Vaccination (AEFI)	Dr. Jacob Puliyel
10.00-10.15	AEFI Causality Assessment Protocol	Dr. L Machado (WHO)
10.15-10.45	Discussion	
10.45 – 11.00	**Tea**	
Session 5 11.00-12.15	**Ethics and Regulations**	**Chair: Dr. Amar Jesani**
11.00-11.15	Data Transparency: Importance of Public Availability of Anonymised Raw Data	Mr. S Srinivasan
11.15-11.30	Compensation For Injury and Deaths in Vaccination	Ms. Sarojini N
11.30-11.45	Rights, Informed Consent in Vaccination	Ms. Veena Johari
11.45-12.15	Discussion	
12.15-13.00	**Lunch**	
Session 6 **13.00-14.45**	**Inclusion of new vaccine in the UIP:** **Cost effectiveness & Financial issues**	**Chair: Dr. Amit Sengupta**

13.00-13.30	Economic Evaluation of Vaccination Programmes	Prof. VR Muraleedharan Dr. Rakhal Gaitonde
13.30-13.45	Implications of Cost on Vaccines	Dr. Ravi Duggal
13.45-14.00	Invited Comment: Criteria for Cost-effectiveness of New Vaccines	Prof. Indrani Gupta
14.00-14.45	Discussion	
14.45 -15.15	**Tea**	
Session 7 15.15-16.30	**Inclusion of new vaccine in the UIP: Health System Preparedness**	**Chair: Prof Mohan Rao**
15.15-15.30	How Robust is Public Surveillance System to Monitor AEFI?	Dr. Jyoti Jain
15.30 -15.45	How Prepared is the System to Deliver Increasing Number of Vaccines?	Dr. MK Aggarwal
15.45 -16.30	Discussion	
16.30-17.30	**Summarising and closing remarks**	**Dr. Amit Sengupta, Dr. Yogesh Jain and Ms. Sarojini N**

Annexure 3: Organisers of the Seminar

The Seminar was organised by Jan Swasthya Sahyog, Sama Resource Group for Women and Health, the National Medical Journal of India and Forum for Medical Ethics Society.

Jan Swasthya Sahyog (JSS) is a collective of health professionals and workers, many of whom have been trained at leading medical institutions in the country like AIIMS. The organisation has been running a health programme in rural Chhattisgarh in central India for the last sixteen years.

Sama is a resource group based in Delhi, working on issues related to women and health. Sama's core work areas include Public Health, Access to Medicine, Bioethics, Ethics in Clinical Trials, Reproductive and Medical Technologies, Gender Based Violence, Sexual and Reproductive Health and Rights, and Mental Health and Young Women.

National Medical Journal of India (NMJI) is a bimonthly peer-reviewed online journal published by All India Institute of Medical Sciences (AIIMS).

Forum for Medical Ethics Society (FMES) is a voluntary organisation born out of an effort by a group of concerned doctors to focus attention on the need for ethical norms and practices in health care in India. It publishes the Indian Journal of Medical Ethics (IJME).

Annexure 4: List of Participants

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