MEETING OF THE NATIONAL TECHNICAL ADVISORY GROUP ON IMMUNIZATION

3 pm-5 pm, Thursday, June 12th, 2014

Nirman Bhawan, New Delhi

AGENDA

Chair: Shri Lov Verma, Secretary Health & Family Welfare
Co-Chair: Dr. V.M. Katoch, Secretary DHR — **Co-Chair: Dr. K. VijayRaghavan, Secretary DBT**
Introduction
Action taken report on last NTAGI meeting, September 23rd, 2013 : Update on progress of pentavalent introduction and strengthening of AEFI surveillance system in country
Agenda items
Introduction of adult JE vaccination in endemic districts
Introduction of rotavirus vaccine
Introduction of IPV in the post-polio eradication phase
Strategies for control of Rubella & Congenital Rubella Syndrome
Other issues for discussion
Recommendations
Recommendations Closing Remarks

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LIST OF ATTENDEES

Chairs & Co-chairs	
Shri Lov Verma	Secretary, Health & Family Welfare & Chair, NTAGI
Dr. V.M. Katoch	Secretary, Department of Health Research & Co-Chair, NTAGI
Dr. K. VijayRaghavan	Secretary, Department of Biotechnology & Co-Chair, NTAGI
Core members, Independent Experts	
Dr. M.K. Bhan	Former Secretary to the Govt. of India, Department of Biotechnology
Dr. Jayaprakash Muliyil	Professor & Head, Community Health, Christian Medical College, Vellore
Dr. N.K. Arora	Executive Director, International Clinical Epidemiology Network (INCLEN), New Delhi
Dr. Parvaiz Koul	Professor & Head, General Medicine, Sher-i-Kashmir Institute of Medical Sciences
Dr. D.K. Taneja	Director & Professor, Community Medicine, Maulana Azad Medical College, New Delhi
Dr. Dilip Kumar Das	Professor, Community Medicine, North Bengal Medical College, West Bengal
Dr. M.D. Gupte	Professor, National Institute of Virology, Pune
Dr. G. Sridharan	Consultant Microbiologist and Virologist, Sri Narayani Hospital and Research Center
Dr. Vinod Paul	Professor & Head of Department, Paediatrics, All India Institute of Medical Sciences, New Delhi
Dr. Arun Kumar Aggarwal	Professor, Community Medicine, School of Public Health, PGIMER, Chandigarh
Core members, Ex-Officio	
Dr. Jagdish Prasad	Director General of Health Services, Govt. of India
Shri. C.K. Mishra	Additional Secretary & Mission Director, National Health Mission, Govt. of India
Dr. L.S. Chauhan	Director, National Center for Disease Control

Dr. Sudhanshu Vrati	Representative of Director, Translational Health Science and Technology Institute, Gurgaon
Representatives from International Partners	
Dr. Nata Menabde	Country Representative, World Health Organization (WHO)
Dr. Genevieve Begkoiyan	Representative of Country Head, United Nation's Children Emergency Fund (UNICEF)
Representatives of Professional Organization	
Dr. Vijay Yewale	President, Indian Academy of Paediatrics, New Delhi
Dr. Ajay Gambhir	Representative of Director, Indian Medical Association, New Delhi
Dr. Ashok Grover	Representative of Director, Indian Medical Association, New Delhi
Dr. Vijaykumar Moses	Representative of President, Public Health Foundation of India
Liasion Members	
Dr. Ajay Khera	Deputy Commissioner, Child Health & Immunization, MoHFW
Dr. Pradeep Haldar	Deputy Commissioner, Immunization, MoHFW
Ms. A. Visala	Representative of Drugs Controller General of India, MoHFW
Special invitees	
Dr. T.S. Rao	Department of Biotechnology, New Delhi
Dr. Ambujam Kapoor	Independent expert
Members of the NTAGI secretariat at Immunization Technical Support Unit (ITSU)	
Dr. Jyoti Joshi Jain	Senior Advisor, Adverse Events Following Immunization, ITSU
Dr. Manish Pant	Senior Advisor, Strategic Planning & System Design, ITSU
Dr. Rajeev Gera	Senior Advisor, Monitoring & Evaluation, ITSU
Apoorva Sharan	Programme Officer, Evidence to Policy unit, ITSU
Amruta Bahulekar	Research Associate, ITSU

Ankur Chabbra	Administrative Officer, ITSU
Others	
Dr. M.K. Agarwal	Deputy Commissioner, Universal Immunization Programme, MoHFW
Dr. Shashi Khare	National Center for Disease Control, New Delhi
Dr. Sunil Bahl	World Health Organization, New Delhi
Dr. Satish Gupta	United Nation's Children Fund, New Delhi
Apologized	
Dr. Rakesh Kumar	Joint Secretary, Reproductive & Child Health, MoHFW
Dr. Gagandeep Kang	Professor, Christian Medical College, Vellore
Dr. Dileep Mavalankar	Indian Institute of Public Health, Gandhinagar
Dr. Y.K. Gupta	Professor & Head of Department, Pharmacology, All India Institute of Medical Sciences, New Delhi
Dr. Indrani Gupta	Institute for Economic Growth, New Delhi
Dr. Jacob Puliyel	St. Stephens Hospital, New Delhi
Lt. General Raghunath	Independent expert, Bangalore
Dr. Chandrima Shaha	National Institute of Immunology, New Delhi
Dr. D.T. Mourya	National Institute of Virology, Pune

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MEETING MINUTES

The National Technical Advisory Group on Immunization (NTAGI) met under the chairmanship of the Secretary, Health and Family Welfare on 12th June 2014. The Secretary, Department of Health Research and Secretary, Department of Biotechnology were present as co-chairs.

The chair and co-chairs welcomed the participants to the meeting and requested all participants to sign and return the Confidentiality and Conflict of Interest agreements to the NTAGI secretariat staff from ITSU. The chair then requested the Deputy Commissioner, Child Health and Immunization (DC, CH&I) to present on actions taken since the last NTAGI meeting and agenda items to be discussed at the current meeting. As per the agenda, the following items were discussed:

1. **Action taken report: Progress report on introduction of pentavalent vaccine in India and strengthening of AEFI surveillance systems in India**

   a) The DC, CH & I updated the NTAGI members present on the progress of introduction of the pentavalent vaccine in India. Following recommendations from the previous NTAGI meeting in September 2013, the pentavalent vaccine has been rolled out in a phased manner in 8 states in India and 11 other states are expected to introduce the vaccine by October 2014. To help prepare states for the rollout of the vaccine, a detailed introductory preparedness checklist has been disseminated among states. Post-Introduction Evaluation (PIE) study, conducted in the additional 6 states where the vaccine was introduced in 2012-2013, indicated preparedness as well as acceptance of state public health systems for immunization.

   b) As recommended by the NTAGI in its previous meeting in September 2013, steps undertaken by the Government of India to strengthen the Adverse Events Following Immunization (AEFI) surveillance system in the country were relayed to the NTAGI. These include the revamping of the National AEFI committee, establishment of an AEFI technical collaborating center viz. Lady Hardinge Medical College and the establishment and operationalization of a dedicated AEFI secretariat. Training workshops have been conducted in states as capacity building measures for improving the quality of AEFI investigation and assessment at state and district level.

   c) The NTAGI was also apprised that the Causality Assessment (CA) sub-committee of the national AEFI committee has evaluated the causality of reported deaths following pentavalent vaccine and found that so far none were causally associated with the vaccine.

   d) NTAGI members suggested that time bound targets for strengthening AEFI and Hib surveillance must be established to ensure that the immunization program is strengthened for introduction of new vaccine antigens.

2. **Agenda Item 1: Introduction of adult Japanese Encephalitis vaccination in endemic districts in India**

a) The NTAGI was apprised of the substantial burden of adult JE in endemic districts in the country, with adult JE cases starting to outnumber cases of paediatric JE in some districts. In this regard, the detailed discussion and recommendations of the Standing Technical Sub-Committee (STSC) were deliberated on by the NTAGI. Following a close examination of the available data on disease burden, vaccine availability and pilot testing results establishing its safety and efficacy in adults as well as other operational issues, the STSC (December 17th, 2013) had recommended the following:

In a context where protection is already likely to be very high, adult JE vaccination campaigns will have to be comprehensive enough to cover the small proportion of susceptible individuals in these endemic areas. Therefore, adult vaccination could be taken up in districts where reliable disease burden data indicates a substantial adult disease burden. A killed vaccine may be used in national program but both doses should, in general, be of the same vaccine in a district. High quality disease burden surveillance should continue.

b) The need for clear definition of "substantial" adult JE disease and establishing operational guidelines to guide effective implementation of the policy, particularly regarding the selection criteria for districts which qualify for adult JE vaccination was stressed. There was general consensus amongst the members that due to the comparatively lower burden of JE (vis-a-vis other childhood diseases) any endemic district with 1 or more confirmed cases of adult JE should be considered for vaccination. Adjoining districts should also be covered for vaccination to account for the possibility of transmission within a given geographical area depending on the vector radius (mosquito) relevant for the JE virus.

c) The importance of confirming the burden of adult JE using reliable molecular diagnostic tests prior to introduction of the vaccine was also stressed. In this regard it was clarified that the cases of adult JE reported in the ICMR safety study were IgM confirmed cases of JE, indicating that there is credible adult JE disease burden data in Sivsagar district. Members recommended high quality disease burden surveillance should continue to inform further policy discussions on the issue.

d) In the context of the interchangeability of the currently used live attenuated SA 14-14-2 vaccine and the newly available inactivated vaccines, the NTAGI endorsed the STSC recommendations that a killed vaccine may be used in the national programme. However, both doses should, in general, be of the same vaccine in a district due to ease of operation, since the three vaccines (one live attenuated and two killed) have different routes of administration and dose schedules.

Recommendation: **Endorsing the STSC recommendation (December 17th, 2013) the NTAGI recommends the introduction of JE vaccination in adult populations in endemic districts based on available evidence of substantial adult disease burden (one or more confirmed adults in an endemic district). Well defined operational guidelines should be prepared (including geographical scope for vaccination if a case is reported in a district) to ensure effective implementation of the policy. Adjoining districts may be**

included in the vaccinations. Any further refinements can be incorporated in this broad recommendation at the ministerial level.

3. Agenda Item 2: Introduction of rotavirus vaccine in India

a) The NTAGI was apprised of the available evidence on burden of rotavirus diarrhoea. Rotavirus is the leading cause of severe diarrhoea in young children and is accountable for an estimated 80,000 deaths, 8.72 lakh hospitalizations and 32.7 lakh outpatient visits in the country annually. (Figures based on 2011 birth cohort, UNICEF India statistics).

b) The NTAGI was also apprised of the safety and efficacy aspects of the three currently licensed vaccines, namely, Rotarix (GSK), Rotateq (Merck) and the newly licensed Rotavac (Bharat Biotech). Data from the use of Rotarix and Rotateq in developing countries indicates that the efficacy of the vaccine ranges from 55%-60% following a complete dosing schedule. The three vaccines have different dose schedules and are not interchangeable.

c) The STSC had undertaken a detailed review of these varied aspects pertaining to the inclusion of a rotavirus vaccine candidate in India in two meetings and recommended the following:

I. In the first meeting (December 17th, 2013) the STSC reviewed the available evidence on avertable burden or rotavirus diarrhoea and recommended that: **The burden of disease, and results from vaccine introduction elsewhere, indicate that India should consider rotavirus vaccination under the universal immunization programme. A detailed analysis of the available vaccines will next need to be undertaken by the NTAGI Standing Technical Sub-Committee. Post-marketing surveillance mechanisms and adverse effects after immunization (AEFI) monitoring will have to be addressed prior to introduction.**

II. In the second meeting (April 21st, 2014 meeting) the STSC conducted a detailed analysis of the safety, efficacy, effectiveness and cost-effectiveness of the three available vaccines and recommended that:

- **An affordable, effective oral rotavirus vaccine should be considered for introduction into the UIP in a phased manner along with close monitoring of impact and AEFIs in particular.**
- **Cost and logistical considerations will be factors in deciding the specific choice of vaccine to be introduced.**
- **The STSC is of the opinion that there is sufficient evidence to introduce Rotavac, the rotavirus vaccine based on the 116E strain, into India's Universal Immunization Programme (UIP). The plans for post-marketing surveillance for Rotavac and the observational studies planned under inter-ministerial oversight were noted and will provide further data on safety.**
- **Considering the known risk of intussusception (IS) posed by rotavirus vaccines, routine AEFI reporting and management systems should be strengthened, and sentinel surveillance systems should be put in place with defined protocols for ascertainment of cases and vaccination status.**

- **The operational considerations that should be taken into account while considering introduction are the feasibility for incorporation into routine immunization and the ability to monitor impact and intussusception.**

d) The NTAGI deliberated on the recommendations made by the STSC in its meetings and while there was general agreement with the recommendations, the committee felt that the newly licensed 116E vaccine is particularly suitable for inclusion in the Universal Immunization Programme (UIP) due to the considerable cost and operational advantages it offered over the other two licensed vaccines (Merck & GSK). The current supply capacity of the vaccine (~ 10 million doses for the year 2014-2015) should be considered when formulating the strategies for the phased rollout of the vaccine.

e) There was a detailed discussion on the safety aspects of the vaccine in the context of the known low risk of Intusussception (IS) following administration of rotavirus vaccines in other countries. Since the trial for the 116E vaccine was not powered to detect any association of the vaccine with an increased risk of IS, the need for establishing clear guidelines and case definitions for monitoring IS and strenghtening of AEFI surveillance systems was stressed. In this regard, the NTAGI was apprised of the Post-Marketing Surveillance (PMS) plans to monitor the safety of the vaccine post-licensure. In addition to the PMS mandated by the DCGI, a self-controlled case series study, as recommended by International Regulatory bodies (WHO, CDC, FDA), has also been planned under the joint oversight of the Ministry of Health and Family Welfare and the Ministry of Science and Technology. The observational study seeks to understand the temporal association between exposure to the vaccine and any adverse event using reported cases, in addition to evaluating issues pertaining to logistics vaccine administration, training of health professionals etc. to develop training modules for future use.

f) There was agreement amongst the members that, due to the burden of rotavirus diarrhoea in India, the inclusion of a rotavirus vaccine in India's Universal Immunization Programme (UIP) would avert a significant amount of diarrhoea related hospitalizations and deaths, despite the reported efficacy of 55-60% of the vaccines in developing country setting.

Following the discussion, Dr. M.K Bhan, recused himself from the decision making process on account of any potential conflict of interest arising out of his involvement with the Rotavac trial.

Recommendation: **The NTAGI endorses the recommendations of the STSC and recommends the introduction of Rotavirus Vaccine in Universal Immunisation Program in phases, in parallel with evaluation of the results of post marketing surveillance and pilot observational study of 116 E strain vaccine.**

4. Introduction of IPV in the post-polio eradication phase in India

a) The NTAGI was apprised of the current status of polio transmission in the country - India has been declared free of Polio in March 2014 following three years of remaining polio free. However, it continues to face the risk of importation, re-establishment of the wild polio virus from endemic countries. In

addition, the risk of paralysis from Vaccine Derived Polio Virus (VDPV) and Vaccine Associated Paralytic Poliomyelitis (VAPP) will remain till the Oral Poliovirus Vaccine (OPV) is being used for immunization.

b) In its Global Endgame Strategic Plan of 2013-2018, the World Health Organization (WHO) recommends a phased withdrawal of OPV, starting with the OPV2 component. In order to mitigate the risk of infection due to reintroduction of WPV2 or CVDPV2 due to OPV2 withdrawal, the WHO recommends the introduction of an Inactivated Poliovirus Vaccine (IPV) in routine immunization programme of countries planning the switch.

d) The STSC deliberated on relevant technical and operational aspects pertaining to the introduction of IPV in the post-polio eradication phase in India in its March 24th, 2014 meeting and recommended the following:

- **India should work towards a withdrawal of OPV2 from the immunization programme and comply with time lines of the globally synchronized tOPV to bOPV switch.**
- **India should introduce a single, full dose of IPV in the routine immunization system in all states, to be given at 14 weeks of age with DPT3. A multi-dose presentation is preferable, but the vial size should not exceed five doses per vial. This should precede the switch from tOPV to bOPV and data for at least one complete year in all states should be available before the switch is made. In areas where RI coverage is low, IPV campaigns can be considered.**
- **Routine immunization strengthening needs to be emphasized to ensure high coverage with all vaccines, including IPV. The inclusion of an additional dose of IPV or a switch to a sequential IPV+OPV schedule should be considered in the future.**

Recommendation: **The NTAGI endorses the recommendations of the STSC (March 24th, 2014) and recommends the introduction of IPV as an additional dose at 14 weeks (with DPT3 & OPV3), tentatively by mid-2015. A comprehensive strategy should be prepared to guide the introduction of IPV in the programme, which should consider, supply capacity, capacity building activities, communication plans etc.**

5. Strategies for control of Rubella & CRS in India

a) India has committed to the elimination of Measles and control of Rubella by the year 2020 in August 2013. In its previous meeting the NTAGI had recommended the introduction of a Rubella Containing Vaccine (RCV) in India's UIP and had requested the STSC to devise comprehensive strategies for the same. Recommendations of the STSC meeting on February 26th, 2014 were presented to the NTAGI for deliberation.

b) Concerns were expressed regarding the introduction of RCV in areas with coverage < 80% and any subsequent rise in CRS on account of the known paradoxical effect of the vaccine in low settings. In this regard, it was clarified that:

- This issue had been extensively deliberated upon at the STSC meeting and the sub-committee had recommended mass catch-up campaigns of all individuals between 9

months- 15 years in the country to counter any potential increase in CRS cases in the country.

- Given the high sero-conversion rates by single dose of RCV, a potential risk mitigation strategy would be to complete catch-up campaigns prior to the roll-out of the vaccine in a particular district.

Recommendation: The NTAGI endorses the recommendations of the STSC (February 26th, 2014 meeting) and recommends the following strategies for the control and eventual elimination of Rubella:

- **Rubella vaccine should be introduced as MR vaccine replacing both doses of the Measles Containing Vaccine (MCV) at 9 months and 16-24 months. All efforts must be made to improve coverage in RI across all states.**
- **To account for any potential paradoxical increase in cases of Congenital Rubella Syndrome (CRS), MR campaigns targeting all individuals from 9 months up to 15 years of age in the country should be conducted as feasible, and future periodicity needs to be decided based on epidemiological data.**
- **Surveillance for rubella is required, both by registries for congenital rubella syndrome and by examining antenatal sera for the proportion of susceptible women, and possibly other age-stratified serosurveys for disease tracking.**

The co-chairs commended the efforts of the NTAGI in considering the evidence and recommending the inclusion of new vaccines in the UIP. While recognizing the far reaching benefits these recommendations will provide to the health of children in India, they also highlighted the responsibility that comes with the decision and extended full support for effective implementation of these recommendations in the country's immunization program.

The chair thanked all the members present for their active contribution and concluded the meeting