National Technical Advisory Group on Immunization
16 June 2008

Minutes and Recommendations

Agenda Items:

A. Use of Thiomersal in multi-dose vaccines

The NTAGI had recommended to the DCG (I) to explore the possibility of use of the lower limit of Thiomersal in vaccines (Indian Pharmacopeia allows the thiomersal content in vaccines of 0.005% to 0.02% as a preservative) and to address the same with the manufacturers. It had also recommended the use of single dose (which doesn't require thiomersal) vials subject to availability of resource for the birth dose of Hepatitis B.

DCG (I) representative briefed NTAGI on this issue. Manufacturers use different concentrations of thiomersal (but within the range specified in the Indian Pharmacopoeia) in different vaccines and the DCG (I) feels that such variations represent the actual concentrations needed as preservative in various vaccines. To reduce the concentration of thiomersal to the 0.005% level manufacturers will have to conduct additional tests and to re-characterize the product and re-validate the production process. The DCG (I) representative felt that the lower limit in the Indian Pharmacopoeia will therefore have to re-examined for adequacy of antimicrobial efficacy. It was conveyed that the DCG (I) is pursuing the issue with all manufacturers and will update NTAGI on the progress, in the next meeting.

Due to constraint of cold chain space and cost of the vaccine current Hep B vaccine is being supplied in multi dose presentation. Following deliberations the following recommendations were made.

Recommendations:

a) DCG(I) to report back (in the next NTAGI meeting) on the validity of the lower limit (0.005%) of thiomersal in all vaccines, the responses from manufacturers, and the reasons, if any, why this cannot be implemented.
b) In view of constraints of cold-chain space and resources, NTAGI supported the continuing use of multi-dose vials for Hep B (birth-dose) for the present.

B. Update on JE Vaccine studies:

NTAGI noted that a major programme on JE vaccination was being implemented using a live attenuated SA 14-14-2 vaccine that has not yet gained wide acceptance globally, and other countries were looking towards Indian experience. Vaccine efficacy with the single dose of this vaccine (as is being currently used in the countries programme) needs to be documented immediately. Safety of this vaccine was preliminarily cleared in the last NTAGI meeting. Longer term and larger denominator safety data are also required and India is in a position to

generate such data on both safety and efficacy. NTAGI was updated on the various studies on live-attenuated JE vaccine:

a) The Adult Viraemia study (does JE vaccine result in viraemia, first in adults and later in children?) is underway and is expected to be completed by early 2009.
b) The Post-Marketing-Surveillance immunogenicity Study has been completed by NIV, Pune, but the result suggested lower than expected values. The test procedures and reagents of JE serology vary from lab to lab and for validation a subset of samples are being tested at another accredited laboratory overseas. The results will be presented in the next NTAGI.
c) The protocol for the proposed case control study to determine the vaccine efficacy/effectiveness in the programme districts has been approved by the expert committee and will be initiated as soon as funds are received. Since MoH has approved funding of this study by PATH no separate approval from the screening committee of the Ministry of Health, will be required. NTAGI requested that funding and commencement of the study be done expeditiously.
d) NTAGI also requested for an update and time-frame on the status of validation of the NIV JE Diagnostic Kit by CDC, Atlanta.
e) The NTAGI proposed that a contract position of a Senior Research Officer (SRO) be provided to ICMR to coordinating and monitor the various JE studies. Funding from DBT may be sought for this position.
f) There was a discussion on the need for establishment and validation of lab tests for vaccine studies and for diagnosis of VPDs pertaining to all vaccines under UIP. Secretary DBT proposed that a work shop (funded by DBT) will be organized in the near future.
g) The need to build-in a suitable disease surveillance system was highlighted

C. Update on Rota virus vaccine:

One rotavirus vaccine is under process of registration and licensing in India. Another indigenous vaccine developed in India is under clinical trail. A sub-committee will be constituted to discuss the disease burden, current information on available vaccines, safety and policy issues on Rotavirus vaccines vis-à-vis the Universal Immunisation Programme. The NTAGI recommended that this meeting be convened over the next 6-10 weeks. A working group may be constituted to prepare the background information for this meeting. ICMR (Dr Ambujam Kapoor) was requested to act as the focal point for the same.

D. Update on introduction of VVM in vaccines:

While MoH accepted the previous recommendations of VVM be added to all vaccine, NTAGI was informed that for the current fiscal year, due to procurement issues, 50% of the vaccine procured will have VVM. From next year all vaccines will be procured with VVMs.

E. Introduction of MMR/MR Vaccines:

Regarding introduction of rubella vaccine, the recommendations of the sub-committee for introduction of MMR/MR vaccine and the India Technical Advisory

Group on Measles mortality reduction (ITAGM) were presented to the NTAGI . A second opportunity for measles vaccine and the introduction of rubella vaccine are specifically for the purpose of reducing measles and related mortality and morbidity as well as preventing Congenital Rubella Syndrome (CRS). Therefore, the impact (outcome) of the interventions must be monitored systematically. This will require appropriate designing of a practical surveillance system for Vaccine Preventable Diseases bridging both public and private sector (who treat a large number of paediatric communicable diseases) health care providers and sensitive towards reporting paediatric VPDs and other communicable diseases. This system could evolve into a more sensitive case based surveillance system at a latter stage.

Following deliberations the NTAGI recommended the following:

a) The NTAGI endorsed the recommendation of the sub-committee to introduce the rubella vaccine in those States that have >=80% MCV1 coverage from recent surveyed data and are able to sustain a routine immunization coverage at or above ≥ 80% .

b) The NTAGI observed that since the 'disability component' of Mumps is not a serious public health problem and since the addition of Mumps component to UIP would result in a substantial increase (more than twice that of rubella vaccine) in cost without commensurate public health benefits, **MR vaccine** should be introduced (in States which are eligible for introduction of rubella vaccine as per (a) above) instead of MMR, at the time of the second dose of Measles for all children at 16-24 months of age along with DPT booster

c) In addition, in these states, Rubella vaccine should be introduced for adolescent girls as recommended by the sub-committee.

d) States introducing MR should also establish surveillance as recommended by the Sub-committee (for monitoring the burden and trend of CRS). The modality of CRS surveillance / monitoring system has to be evolved and the subcommittee was requested to develop designs for the purpose and to report the same in the next NTAGI meeting.

F. Recommendations of the Measles ITAGM (September 2007)

The NTAGI deliberated on the ITAGM recommendations and accepted them in principle. NTAGI members wanted to know the rationale behind selecting the appropriate target age group for the measles catch-up campaigns. It was clarified that measles epidemiological data from six states in India show that more than 90% of the measles cases occur in children below ten years and SIAs in general should target this age group.

NTAGI also considered the available data on measles case fatality ratio(CFR) in India and recommended the following:

a) A second dose of Measles should be introduced in UIP (with DPT booster) in states with > =80% evaluated MCV1 coverage by the most recent survey (CES-2006).

b) Catch-up measles SIA campaigns should be implemented for children upto 10 years in states with <80% evaluated MCV1 coverage. Detailed action plans for these SIAs are to be finalized immediately prioritizing states with low MCV1 coverage and high measles mortality burden.

c) In view of convergence with Polio eradication activities in UP, a decision on catch-up SIA for Measles is to be taken after consultation with State Government.

d) To inform the UIP program on more reliable estimates of measles mortality, studies on measles case fatality ratio will be conducted in selected high burden states.

e) Expansion of measles surveillance will be done in UP and Bihar and other states with high mortality due to measles for SIA planning and having a baseline.

G. Introduction of Haemophilus influenza B and Pneumococcal vaccine:

The previous NTAGI had recommended that a sub-committee on Hib vaccine be convened to look into the introduction of Hib vaccine in UIP. At a meeting held at MoH on 10 March 2008, the Secretary had suggested that the same sub-committee also look into introduction of Pneumococcal vaccine.

A meeting of NTAGI sub-committee on Hib & Pneumococcal vaccine introduction in India was held on 16th and 17th April 08 at ICMR Delhi. The recommendation of the sub-committee was presented to the NTAGI. The NTAGI deliberated on the various issues and endorsed the recommendations of the sub-committee and further recommended the following:

a) The time-line for the National roll out of Hib vaccine as proposed by the sub-committee by 2012 be expedited. HIB vaccine be introduced immediately throughout country in all the States.
b) Depending on the vaccine availability the Hib vaccine should be introduced as a multi-dose liquid pentavalent vaccine (DPT-Hep B-Hib).
c) A small working group be constituted as early as possible for development of action plan and to coordinate the roll-out of pentavalent vaccine.
d) The proposed Impact Study on Hib (Pentavalent vaccine) and Pneumococcal vaccine (PCV 7) introduction in one high mortality State with adequate cold chain space should be initiated as soon as possible
e) Impact studies related to new vaccine introduction should be built into the programme
f) NTAGI approved the request from ICMR to publish the NTAGI Sub-committee on Hib recommendations in any journal.

H. Strengthening of Human resources and Physical infrastructure

a) A high-level HRD Committee that has been constituted to look into the man power needs for bringing about transformational change in UIP to provide recommendations to Govt of India.
b) IPHS for facilities and other management structures to be modified to include manpower, equipment & other infrastructure needs for immunization programme.

I. Discussion on strategies for sustaining eradication after cessation of wild polio virus circulation:

Following discussions it was recommended to ICMR to constitute a group to prepare the strategies for sustaining eradication after cessation of wild polio virus circulation.

J. Recommendations on other issues relating to UIP:

a) A formal NTAGI support group to be formed by ICMR/GoI to provide on-going technical support and to prepare necessary documents for the NTAGI.
b) On the issue of introducing DPT instead of DT at 5 years of age, the NTAGI on the basis of deliberations recommended the use of DPT instead of DT.
c) BCG schedule to remain same till more data/evidence are provided by IAP for justifying the change of schedule.

K. Hep. B – implementation and studies

a) Hepatitis 'B" vaccination has been started in all the districts of 11 states, except Chhattisgarh and West Bengal.
b) The Seroprevalence study to determine the impact of Hepatitis 'B' vaccination and studies of HBeAG as recommended by NTAGI will be conducted by ICMR.

L. Constitution of body to look into R&D and vaccine development in public sector unit.

It was recommended that DG (ICMR) and Secretary (DBT) constitute a body that will look at R&D and vaccine development in public sector and fund these studies as a priority.

M. Recommendations on other matters:

A formal NTAGI support group to be constituted by ICMR/GoI to provide on-going technical support and to prepare necessary documents for the NTAGI. This may require recruitment of technical staff and Dr Ambujam Kapoor was authorised to initiate appropriate action towards the same. Secretary DBT agreed to provide the necessary funds for this purpose.