T-13013/01/2018-Imm
Government of India
Ministry of Health and Family Welfare
Immunization Division

Nirman Bhawan
Dated: 17th July 2022

To,

NTAGI members/Participants
(As per list enclosed)

Subject: Minutes of the meeting of 17th National Technical Advisory Group on Immunization (NTAGI), held on 28th June 2022, under the Chairpersonship of Secretary (Health & Family Welfare) at Nirman Bhawan, New Delhi

Sir/Madam,

Please find attached herewith the minutes of the 17th National Technical Advisory Group on Immunization (NTAGI), held on 28th June 2022, at Nirman Bhawan, New Delhi under the Chairpersonship of Secretary (Health & Family Welfare), for your kind perusal.

Yours Faithfully

Enclosure : As above

Dr. Veena Dhawan
Additional Commissioner (UIP)

Copy to:

1. Sr. PPS to Secretary (H&FW), MoHFW
2. PPS to DGHS, MoHFW
3. PPS to Secretary (Department of Health research), MoHFW
4. PPS to Secretary (Department of Bio-technology), MoS&T
5. PPS to AS&MD (NHM), MoHFW
6. PPS to JS (RCH), MoHFW
7. Office copy

17th National Technical Advisory Group on Immunization (NTAGI)Meeting
June28, 2022, Tuesday, 11:00 AM to 01:30 PM
First Floor, Room # 155-A, Nirman Bhawan, MoHFW, New Delhi

Minutes of the Meeting

Welcome & Introduction

The 17thNTAGI meeting was held on Tuesday, June 28, 2022 at MoHFW, New Delhi, under the Chairpersonship of Shri Rajesh Bhushan, Secretary Health & Family Welfare (H&FW) and co-chairpersonship of Dr Balram Bhargava, Secretary, Department of Health Research & Director General, Indian Council of Medical Research (ICMR) and Dr Rajesh S. Gokhale, Secretary, Department of Biotechnology (DBT).

All participating NTAGI members and invited attendees had duly filled and signed the confidentiality agreement, and declared conflict of interests (if any), and shared them with the NTAGI Secretariat. The list of attendees is Annexed as **Annexure-1** and agenda as **Annexure-2**.

It was informed that the minutes of the NTAGI meeting held on May 28, 2021 were shared with the members and no comments were received. The minutes were formally confirmed by the NTAGI.

Opening Remarks

All participants were welcomed by the Chairperson and Co-Chairpersons. Shri Rajesh Bhushan, Chairperson informed the purpose of the meeting. At the outset he thanked members of the COVID-19 WG and NTAGI-STSC for continuous guidance on various issues pertaining to COVID-19 vaccines.

Both the Co-chairpersons of the NTAGI, Dr Balram Bhargava and Dr Rajesh S. Gokhale also appreciated the work done by the COVID-19 WG in past two years. It was shared that since the last NTAGI meeting, eleven NTAGI-STSC meetings were held and following agenda items were discussed: JE vaccines working group proceeding and recommendations which were endorsed by the NTAGI-STSC, Typhoid vaccine working group proceedings which were endorsed by the NTAGI-STSC, HPV vaccine WG proceedings, interchangeability of rotavirus vaccines, COVID-19 vaccine WG proceedings, where recommendations on additional dose, priority pediatric population for COVID-19 vaccines, mix-match of COVID-19 vaccines for boosters, Sputnik V vaccine, ZyCoV-D vaccine, Corbevax vaccine, pediatric data of Covaxin and Covovax vaccines, NCDC COVID-19 mortality data, COVID-19 vaccine tracker and CMC Vellore's Covaxin and Covishield mixed booster study were discussed.

The Chairperson introduced new DGHS, Dr Atul Goel. Following agenda items were discussed:

Agenda Item 1: Action Taken Report on previous NTAGI meeting held on May 28, 2021: JS-RCH

Dr P Ashok Babu, Joint Secretary-RCH informed that the last meeting of NTAGI was held on May 28, 2021. The action taken report (ATR) based on the recommendations made in the previous NTAGI meeting, were presented.

Japanese Encephalitis (JE) Vaccines: The members and invited attendees of the meeting were apprised that efforts under RI and IMI have resulted in improvement of JE vaccination coverage to 81%. Data on age stratified JE cases linked with vaccination status is currently not being collated. The NCVBDC has sent a communication to all states for sharing this data. A review of epidemiological data to see the need of the boosters after 5-7 years, in different ages and regions will be done by JE Working Group. As of date there are total 336 JE endemic districts, 39 new districts were notified in the previous financial year. Campaigns

for children have been completed in 301 districts of 21 states. Adult campaigns have been completed in 40 districts of 3 states. Jeev vaccine is being used in 08 states and Jenvac vaccine is being used in 13 states. The M/s Biological E is planning for a Clinical Trial to assess the Equivalence of Indian (Jeev) and international (XIARO) products for age group of 2 months to 80 years. M/s Bharat Biotech has competed the recommended study, results will be presented to JE WG once the analysis is completed. It may take three to six months to do immunogenicity analysis of serum samples. The JE interchangeability study: Ethical approval has been obtained from 8 out of 9 sites. Study will be initiated after approval of ICMR finance division. In reference to missing of scheduled dose of Jeev vaccine, the 32nd NTAGI-STSC recommended that a 3-µg formulation of Jeev vaccine may be used till the age of 5 years. A catch-up campaign may be done every five years to cover missed population of children above 05-15 years using 6-µg dose.

National Vaccine Tracking Platform: Based on the 16th NTAGI recommendations a vaccine tracker platform was developed by ICMR. Details of challenges faced for making it functional and suggestions for its modification to facilitate NTAGI work will be discussed in a new Working Group consituted under NTAGI-STSC.

Mix-Match dosing studies: It was informed that the CMC Vellore has conducted a mix-match booster doses study. Results will be presented as part of the NTAGI-STSC deliberations.

COVID 19 Vaccination for pregnant and lactating women: Following the 16th NTAGI recommendations, an all-stakeholders consultation workshop was organized in June 2022. Operational guidelines and communication tools were developed and disseminated. Vaccination started on July 02, 2021. As of June 22, 2022, CoWIN platform data, 16,85,587 women tagged as Pregnant women have received first dose, 14,07,383 have got second dose and 599 received precaution dose. No separate data of lactating women is generated. In order to monitor safety of COVID-19 vaccines in pregnant women 20 sites in 20 states, including North-East states, have been identified across the country, study is expected to commence from next month.

Discussion

A member raised concern over slow uptake of COVID-19 vaccines among pregnant women. The chairperson clarified, that the data on CoWIN platform is of women who were tagged as pregnant. However, in many instances information on pregnancy may not have been captured by vaccination team and due to that even if a large number of pregnant women might have received vaccine but could not be tagged as pregnant women on CoWIN. Furthermore, it was informed that till date 53 crore women have been vaccinated, out which 38 crore are of reproductive age group (15 to 45 years). The annual cohort of pregnant women is around 2.9 crore. In addition, it was clarified that there has not been any difference in vaccine uptake in rural and urban areas. It was emphasized that the communication strategies may be refined to improve the precaution dose coverage. Based on evidence transition may be done from precaution to booster dose.

Another member requested if the interim results of Jenvac vaccine study are available. It was informed that immunogenicity analysis of the serum samples has been initiated by the M/s Bharat Biotech and results are expected in next 3-6 months.

Agenda Item 2: Typhoid Vaccines: Chairperson, Typhoid Working Group (TWG)

Dr Gagandeep Kang, chairperson, Typhoid working group presented burden of typhoid fever in country, antimicrobial resistance, efficacy/effectiveness and safety of available Typhoid Conjugate Vaccines (TCV), and cost-effectiveness of the vaccines. In 12th NTAGI meeting, held on December 09, 2016, it was recommended to enhance typhoid surveillance to inform future discussions and recommendations on typhoid vaccine use in India. It was recommended to generate contemporary data on typhoid burden in community and hospital-based settings, age-specific incidence of typhoid disease data and geographical distribution of typhoid disease data in country. Based on the NTAGI recommendations Surveillance for Enteric Fever in India (SEFI) Consortium was formed which had 18 sites across the country. It was set up to assess incidence of typhoid fever, its consequences and impact of interventions. Findings of SEFI study, Navi Mumbai TCV implementation study, evidence on antimicrobial resistance, and cost-effectiveness of TCV were first reviewed by the TWG in three meetings and then presented in the 40th STSC.

The gold-standard for typhoid diagnosis is blood culture, which has ~60% sensitivity. Prior intake of antibiotics decreases sensitivity of blood culture. Places where blood culture is done, they get sample of patients after antibiotics are started. Pattern of short cycle and long cycle transmission may differ in patterns. In tier I of the SEFI, 6000 children of age 06 months to 15 years were followed up for fever every week, and blood culture was done if fever lasted for ≤3 days in the community of Delhi, Pune, Kolkata and Vellore. Based on the WHO classification, the incidence of typhoid fever was very high (>500 per 100,000 CYO) in Delhi (576), Kolkata (714) and Vellore (1173). In Pune (35) which was a rural site the burden was moderate (10-100 per 100,000 CYO). Important point to observe was that antibiotic usage at this site was> 2.5 times that seen in the other cohorts (11.8% Vs.4.5%). Incidence is high in the age group of 01-15 years but peaks up in in the age group of 05 to 09 years. In tier II, six sites were added for hospital-based surveillance of typhoid fever for children as well as adults. This tier captured fevers that presented at a health care facility and therefore reflect severe typhoid fever. In ≤15 years old, incidence was very high in two sites (Chandigarh and Anantapur), high in another two (Nandurbar and Kullu), moderate in one (Karim Ganj) and borderline moderate in one (Raxaul). Reason for borderline moderate in one was an issue with not having enough blood cultures in children before they received antibiotics. Among adults, all sites had high incidence and Chandigarh had very high incidence. Overall, in ≤15 years old children, incidence was very high in all urban sites, high in two rural sites, moderate in two rural sites and borderline moderate in one rural site. In tier III, major hospitals in the country were included to see severe typhoid complications and AMR. Total eight hospitals including two children's hospitals were part of this study. There was a high rate of reporting of typhoid cases. In absence of denominator, actual incidence rate cannot be calculated, but the complications of typhoid, such as intestinal perforation, were reported. Of the 158 nontraumatic ileal perforation cases identified, 126 were consented and enrolled. Enteric fever (34.7%), Tuberculosis (19.0%), malignancy (5.8%), and perforation of Meckel diverticulum (4.9%). In those with enteric fever ileal perforation, the CFR was 7.1%. Enteric fever remains the most common cause of nontraumatic ileal perforation in India, followed by tuberculosis.

Ceftriaxone is the first line of treatment in northern India and azithromycin in southern India. Plasmid mediated resistance with ESBL gene is a cause of concern. Azithromycin MIC increasing in S. Typhi. Classically defined MDR is decreasing. In neighboring countries emergence of azithromycin resistance S. Typhi and outbreaks of XDR S. Typhi have been observed recently which is a matter of concern. In India, two isolates from Gurgaon*, S.* Typhi closely related to 2016 XDR *S.* Typhicarried *bla*$_{\text{CTX-M-15,}}$ *bla* $_{\text{TEM-1D}}$ and *sul2*, *dfrA and* belonged to 4.3.1 (H58 lineage I) lineage, two isolates from Tamil Nadu with *bla*$_{\text{CTX-M-15}}$ and four isolates from Mumbai, and one from Vellore with *bla*$_{\text{SHV-12}}$*bla*$_{\text{TEM-1B.}}$ Close monitoring is needed.

In India, there are four indigenous Typhoid Conjugate Vaccines licensed by CDSCO. One is for ≥6 months to ≤ 65 years, with efficacy from 81.6-97%, another two for ≥6 months to ≤ 45 years, and the fourth one is for ≥6 months to ≤ 65 years with 100% efficacy. Two vaccines have received WHO prequalification status. None of the vaccines have shown safety concerns and have good immunogenicity. Clinical Trials, in Bangladesh, Malawi, Nepal and Navi Mumbai implementation study have shown that TCV is highly effective. All these trials were in campaign mode; therefore, longevity of protection is not known.

Protective efficacy of five years, 10 years or 15 years was modelled. It showed that vaccination strategy was 99%-100% cost effective in urban areas in all three scenarios when indirect cost was considered. Urban vaccination strategy was cost-saving too. In rural settings of India, it was not cost-effective strategy as in urban areas if indirect costs were not included.

In 2018, WHO made a recommendation on introduction of TCV in countries having high burden of typhoid fever.

In the 40th STSC meeting following recommendations were made by the STSC:

- In view of very high burden of typhoid disease, time required to reach optimal level of WASH and impact of vaccination of antimicrobial resistance, a typhoid conjugate vaccine may be introduced under the Universal Immunization Program. The vaccination drive may be done in phases. The first phase may be of five years and based on the impact of phase 1, future strategy may be adopted.
- Surveillance of the cases, severe typhoid and post-vaccination breakthrough infection and antimicrobial resistance may be continued at multiple sites, particularly to monitor impact. Continue surveillance and conduct TCV impact assessment 4 years after introduction to decide on strategy for phase 2. AMR continues to require monitoring and the emergence of new resistance patterns may also necessitate moving beyond routine immunization for selective campaigns.
- The TWG may develop a clear strategy for including age at vaccination and priority states for initiating introduction of Typhoid vaccines in view of manufacturers' capacity, and plan of scaleup in Phase 1 and present at the next STSC. In addition, strategies for future phases if required.

In the 41st STSC meeting the TWG presented different strategies for introduction of the TCV in UIP. In a ten-year horizon if nothing is done then there will be 4.6 crore cases and 89,300 deaths. Very high and high burden in almost all age groups of urban areas and in young adults in rural areas has been estimated. Campaign and Routine for all will help in reducing maximum number of typhoid cases, followed by school-based campaigns and routine for all, and then only urban campaigns and routine for all. Campaigns may be

helpful in reducing similar burden 3-4 years faster in comparison to routine only strategies (only urban and all).

In the 41st STSC meeting following recommendations were made by the STSC in order of preference:

- Initiate routine vaccination along with MCV at 9-12 months. One-time school-based campaigns for all children (urban and rural), and vaccination at school entry for next three years. (Includes campaign)
- Routine vaccination along with MCV at 9-12 months with one-time urban school-based campaigns. (Includes campaign)
- Routine vaccination along with MCV 9-12 to be introduced, and for 4 years at school entry and in class 5th (along with HPV vaccine?); for next five years. (No campaign strategy)

Discussion

The chairperson thanked TWG and STSC for exhaustive work on typhoid and open the floor for discussion.

A member raised concern that the typhoid vaccine may be useful to protect individuals and may not be helpful in preventing exiting of bacterium from gut. It was informed that human challenge studies have shown reduction in transmission when challenged with 10,000 live bacilli. The TCV will reduce quantum of transmission as well reduce the burden of disease if the vaccine is introduced in routine immunization under UIP. There has been a revolution in the field of vaccine when conjugate vaccine arrived, it has been seen in case of Hib vaccine, and PCV. It happened because polysaccharide was conjugated to a protein and changed nature of immune response.

One of the members requested if the SEFI study was hospital based or community based. It was informed that in tier 1, a cohort of 24000 children were followed up for two years for more than three days fever in the community. In tier 2, small hospitals of remote area were included which represented community. In tier 3, large hospitals were included where denominator was not available for calculating incidence in community.

In response to the query related to genome sequencing data on transmission of the S. Typhi strains from the country to other parts of the world, it was informed that the it was based on historical collection of S. Typhi isolates stored in different laboratories. Genetic sequencing was done very recently. As strain evolve with time, therefore by looking the sequences, it can be found when strain changed and their relatedness. It was based on the linking of strains found in other parts of the world with strains found at different times in India.

Members agreed that India is a high typhoid endemic country, there is enormous antibiotic misuse and there is antimicrobial resistance. On introduction of the TCV in UIP, eradication of the disease may not be possible in a short phase, but it will help in bringing down the burden of disease and may also help in dealing with AMR.

Issue of over-the-counter antibiotics and prescription practices was highlighted. Furthermore, it was mentioned that due to wide scale development around the country distinction between rural and urban areas is fading, therefore, the disease confined to urban areas are expected to be present in rural areas as

well. It has been observed in case of Hepatitis E also. It was mentioned that it is a great opportunity to introduce the TCV where public health impact could be seen in next three-four years.

In response to a query, it was informed that on food handlers, studies that are done in India have looked in populations for carriers, there is very little carriage that has been found. Studies have also been done in people with gall-stones, because biliary carriage is supposed to be a key part of transmission. With the use of new antibiotics, it is difficult to find people that are typhoid carriers. It was stated that a short-term shedding occurs shortly after disease but usually resolve by the end of two weeks. It was mentioned that there is no known reason to suggest higher carriage in food handlers than general population.

Dr Rajesh S. Gokhale, Co-chairperson, solicited reasons for higher burden of typhoid fever in children. It was informed that the fact of children has higher burden is due to higher exposure and susceptibility. In case of typhoid, where exposure is high, younger population is more affected. Furthermore, where, exposure is low, there older population is mostly affected.

Dr Balram Bhargava, Co-chairperson, shared that it is evident that there is burden of disease, effective vaccines are available which are found to be cost-effective. Now, it is important to choose between one of the suggested strategies for introduction.

Shri Rajesh Bhushan, Chairperson, summarized the discussion and shared that the vaccines are safe, effective and cost-effective. Furthermore, it was suggested that immunization program division may deliberate and choose one of the strategies for introduction of the vaccine in the UIP.

Recommendation

Based on the presentation the NTAGI endorsed the recommendations of the STSC on TCV with following:

- Indigenous Typhoid Conjugate Vaccines are safe and efficacious and there is sufficient burden in the country to consider this disease as a public health problem. Therefore, it is worthwhile to introduce Typhoid Conjugate Vaccine in the universal immunization program.
- Program managers at Immunization Division may consider one of the recommended strategies on introduction of the Typhoid Conjugate vaccines in Universal immunization program.

Agenda Item 3: HPV Vaccines: Chairperson, HPV Working Group

Dr NK Arora, Chairperson, HPV Working Group shared those recommendations on HPV vaccine introduction were already made by the NTAGI in its 13th meeting held on December 19, 2017. In the 39th STSC meeting HPV WG was reconstituted to review available evidence on disease burden, effectiveness of single dose, clinical trial data of domestically developed HPV vaccine, best age for vaccination, and cost-effectiveness of HPV Vaccine. The HPV WG presented a report in the 41st NTAGI-STSC.

Almost 12% of the HPV related cancers occur in India. Based on data from 28 Population Based Cancer Registries (PBCR), highly variable incidence of cancer cervix (Ca-Cx) in India – 27.7 to 4.8 per 1,00,000 population. The incidence starts rising in the age band 30-35 (3/100000) to peak at 65-69 (50/100000) and declining thereafter Significant decline in annual incidence of Ca-Cx since 90s despite lack of any specific intervention programs (Screening and Vaccination). Concurrent with declining Ca-Cx, the breast cancer incidence is increasing. Based on the current trend, India is likely to diagnose over 85,000 Ca-Cx cases in

2025. Prevalence of HPV 16/18 in different clinical states: Normal – 5%; Low grade cervical changes – 28.2%; High grade cervical changes – 62.8%; and Cervical Cancer – 83.2%.

Sikkim is the first state to introduce the HPV vaccine in entire state. There average age adjusted incidence rate (AAR) for Ca Cervix was 10.1 / 1,00,000 women in (2012-13). PBCR report of 2015 & 2016 showed 11.52% and 9.41% Ca Cervix of total Cancer cases. Initially, the vaccine was introduced in 2014 but could not be continued due to hesitancy. Later, the vaccine was re-introduced in 2018 after detailed pre-roll out preparation and leveraging lessons of 2014. All 9 to <14 years old girls were given 2 doses of vaccine separated by minimum gap of 6 months. All Schools were included (Government as well as Private) and out of school girls of this age group covered with a total cohort of 25,284. Campaign duration was of 2 to 3 weeks: Initial one week vaccination in all schools / educational institutions and 2nd week in health facilities for drop out children and out of school beneficiaries. The coverage of first and second round was 96.69% and 97.85% respectively. The routine vaccination coverage in 2020 was 88.5%. The Key lessons from Sikkim HPV vaccine introduction include strong political will and media sensitization to ensure smooth roll out of the campaigns. Parent-teacher meetings in all schools and one teacher made as nodal person for HPV vaccination. Same class vaccination was a favorable strategy for second dose vaccination after six months. Series of media workshop by involving senior doctors for media discussion and mass communication.

Recently SAGE has made following recommends by updating dose schedules for HPV, these include:

- One or two-dose schedule for the primary target of girls aged 9-14
- One or two-dose schedule for young women aged 15-20
- Two doses with a 6-month interval for women older than 21

For Immuno-compromised individuals, including those with HIV, SAGE as recommended three doses, if feasible, and if not at least two doses. There is limited evidence regarding the efficacy of a single dose in this group.

The HPV WG recommended a single dose HPV vaccine having at least 2 years evidence on sustained and adequate antibodies level and efficacy/effectiveness data after single dose, is recommended for the girls of age 09-14 years in routine immunization. Preparation for the roll out plan has to be based on the lessons of the Sikkim experience. Social mobilization and IEC absolutely essential. CoWIN like platform might be used in tracking of vaccine recipients if in future there would be need of second or third dose of the vaccine. Immuno-compromised individuals may be given two doses of HPV vaccine with minimum interval of six months between the two doses. Consideration of catchup campaigns: Contingent on the availability of vaccine. A one-time catchup for 9–14-year-old adolescent girls followed with routine introduction at 9 years.

Routine introduction at 9 years and taking one year-age cohort every year 14 years backwards for next two to three years to take care of the missed cohorts for catch up at this time. Immunization of boys is recommended once 80% routine immunization coverage is achieved in girls.

Policy questions that will guide for different economic evaluation studies are required considering variation in disease burden across country, treatment access, outcome and vaccine acceptance. Dr Indrani Gupta and

Dr Rakesh Agarwal will articulate some policy questions and bring these to HPV WG for finalization; Dr Shankar Prinja to be invited who did the first economic evaluation for the HPV Working Group. The HPV WG further suggested following research studies: Factors for declining incidence Ca-Cx incidence in the absence of any systematic interventions need to be understood. Oral, Anal, Oro-pharynx Cancers are also HPV related but the contribution of HPV not worked up in India, a study need to be conduct to assess it. Single dose will be off label and hence requires inbuilt studies for monitoring the effectiveness of the vaccines and also the impact. In certain geographical regions Cohorts may be followed up for persistence of HPV antibodies over next 5-10 years. Monitoring of evidence of CIN or other evidences of HPV 16/18 colonization is needed. Vaccines with no data about the sustained and adequate antibody levels for 24 months after a single dose will require cohort studies to monitor the antibody levels after roll out in the program.

The NTAGI-STSC endorsed the HPV WG recommendations with following:

- The HPV WG may engage with the manufactures to understand their manufacturing capacity and inform them about expected data
- The Indian manufacturer may be asked to initiate a follow up of neutralizing antibodies titers in Phase I and II participants
- The HPV WG may plan a study to understand various aspects of programmatic challenges and facilitators in early introducing states.

A presentation was made by M/s Serum Institute of India. The HPV WG, has requested some additional data from manufacturer that will be reviewed in next HPV WG meeting.

Discussion

The Chairperson requested course of action taken by the WHO following the SAGE recommendations. It was informed that the DG WHO has accepted the recommendations of SAGE. A WHO position paper is being prepared and it is expected to be published in next two months. Furthermore, it was shared the first WHO position paper came in 2014, which was updated in 2017 and now it is again updated. In this paper, previous recommendations of two dose regimen have been changed to one or two dose. This recommendation stands for the vaccines for which data is available on single dose showing one dose regimen was equivalent to two dose regimens for use in national immunization program.

The Chairperson also solicited on the data requested by the HPV WG from the manufacturer. It was informed that the WG has requested age stratified immunogenicity data of SII vaccine and Gardasil vaccine, sub analysis of antibody levels for all four types, and comparison of PBNA immunogenicity and safety data between vaccine arm and control arm.

In response to a query on SAGE recommendations it was shared that the chances of getting optimum antibody response after single dose are higher in younger age groups when compared to older age groups. Therefore, if a girl gets a single dose at the age of twenty years may not need second dose at the age of 21 years. Furthermore, it was shared that the SAGE recommendations are for those vaccines for which data is available for one dose is available. These include Merck and GSK vaccines. These vaccines have evidence of

antibody production, stability of antibodies for long period (at least 2 years), and infection prevention. In case of SII vaccine evidence of antibody production is available.

A member suggested prioritization of vaccine in North-Eastern states as burden of HPV associated cancers is very high in both male and female in those states. Another member stated that reason for prioritization of girls for vaccination is based on the attributable fraction of HPV in cervical cancer is highest.

It was suggested that as the recommendations for introduction of the HPV vaccine in UIP were already made by the NTAGI in 2017, the SII vaccine may be introduced as per the licensed indication in addition to generating research evidence. It was also suggested that as seen in Sikkim, the program may engage with all stakeholders to ensure that vaccine is well received.

The chairperson and co-chairpersons agreed that the indigenous vaccine may be introduced in the program as a two-dose regimen as data on single dose is not available yet. The HPV WG may quickly review the requested evidence and share its report.

Recommendations

The NTAGI endorses recommendations of the STSC on HPV vaccine with following:

- The indigenously developed qHPV vaccine may be considered for introduction in the UIP as a two-dose regimen as indicated in product insert, once the HPV WG satisfactorily reviews the requested data
- A study may be conducted to see immunogenicity, persistence of adequate antibody levels and protection from infection after two years of a single dose indigenously developed qHPV vaccine administered to a cohort of girls
- In the UIP, a mechanism may be developed to follow-up girls who may have received only one dose in the program and do not come back to receive second dose as recommended. Their samples may be collected after two years and real-world immunogenicity and effectiveness data of single dose may be generated

Agenda Item 4: Covid-19 Vaccines: Chairperson, COVID-19 Working Group

Dr N K Arora, chairperson, COVID-19 WG (CWG) shared that the issues pertaining to COVID-19 WG have been discussed in 23 CWG and 11 STSC meetings since the previous NTAGI meeting. Evidence on Sputnik V and Sputnik light vaccines, Corbevax vaccine, ZyCoV-D vaccine, pediatric data of Covovax and Covaxin vaccines, COVID-19 mortality data in children, priority pediatric population for COVID-19 vaccines, additional dose for immunocompromised individuals including renal transplant patients, time interval between primary series and booster dose, CMC Vellore's Heterologous/Homologous booster study, COVID-19 Vaccine tracker, and feasibility of updating CoWIN portal for people who had completed full/partial primary series and/or booster from another country.

Sputnik V vaccine may be considered for interchangeability studies with other available vaccines. Sputnik light as a precautionary dose to eligible population. Operational study may be conducted to understand various facilitating factors and challenges in implementation of new generation of vaccines requiring ultra-cold storage.

Corbevax may be administered to pregnant and lactating women along with adults in general vaccine. As evidence from DART studies suggest that the vaccine is safe. The vaccine is immunogenic and safe for children 12-18 years and 05-12 years. Effectiveness and safety data of the vaccine in actual program settings for all the vaccines particularly for Paediatric age group is needed; introduction in the younger population (<12 years) should be introduced when system for monitoring safety and impact assessment is in place.

Covaxin has no safety concerns in children of 6-12 years. The vaccine is already being used in 15 to 18 years since January 22. Effectiveness and safety of the vaccine in program settings need to be determined.

ZyCoV-D vaccine was recommended for adults in December 2021, where it was suggested to implement in limited geographical population. May not be administered to pregnant and lactating mothers until substantial safety data from other adult population is made available. As of May 2022, more than 26000 subjects (including more than 1000 adolescents) completed 12 months follow-up. The vaccine was found to be well tolerated by both adolescents and adults. None of AEs lead to discontinuation of vaccine. There were no vaccine related SAEs. Furthermore, none of the adults/adolescents tested for ANA, developed any of the ANA antibodies. Sero conversion rates of IgG and NAb of 2 mg, 3 dose vaccination schedule and 3mg, 2 dose schedule were observed to similar in adults as well in adolescents. The CWG recommended 2-dose schedule of ZyCoV-D for children in the age group of 12-17 years should be included in the COVID-19 National COVID-19 Vaccination Program.

Covovax data of day 36, showed 98.8% sero conversion rate. No AESI has been reported. Overall, vaccine is observed to be safe, 84 days after the second dose. The CWG recommended COVOVAX COVID-19 vaccine for the children of age 12-17 years.

Priority Comorbid conditions identified based on review of literature of risk factors for severe disease/ death due to COVID-19 in children:

- Type 1 Diabetes receiving insulin therapy
- Heart diseases: Congenital/Rheumatic
- Immunocompromised/ immune-deficient patients
- Children on dialysis; awaiting renal transplant
- Children with chronic liver disease; awaiting liver transplant
- Morbid/ severe obesity (Adult equivalent for Morbid: BMI> 40 kg/m_2 ; Severe: BMI >35)
- Neuro-developmental disorders: Life-limiting neuro-disability/ complex neuro-developmental disability
- Chronic respiratory diseases: Uncontrolled severe persistent asthma (defined below) and Chronic lung diseases (Interstitial lung disease/ Cystic Fibrosis)

The NCDC presented data on age wise distribution of deaths reported to NCDC in 2020, 2021 and 2022 where age stratified data was available. In 2022, age stratified data of only 800 cases was available, from more than 42000 deaths. Lag in district level case and outcome data sharing is one of the important reasons behind the limited age distribution data availability. Children with and without comorbidities have

different outcome with COVID 19 infection. This information is not available but case reports indicate worse outcome with comorbidities.

The NTAGI-STSC considered the worthiness of COVID-19vaccines in under 12 years population. However, a decision of introducing the vaccine in this age group may be taken by the NTAGI. The NTAGI-STSC recommended setting up a working group to look into future solutions for cross talk across three databases and development of robust vaccine impact assessment and safety monitoring platform.

In reference to additional dose, it is reiterated that the issue of additional dose to immune-compromised has already been discussed in depth and the MoHFW should take a decision in view of the recommendations already made by the 36th NTAGI-STSC meeting held on December 06, 2021.

The scientific evidence from CMC Vellore study suggested that Covishield booster dose given 6 months after COVAXIN primary series gives 6-10 times higher antibody level as compared to when Covaxin is administered as the booster dose after a gap of six months after the primary schedule. Furthermore, surrogate neutralization to multiple variants showed ≥90% increase in NAb for all variants other than omicron, when Covishield was administered as booster after Covaxin primary series. Against Omicron variant significant jump of 60% NAb response was observed. This type of NAb was not observed when Covaxin was admisntered as booster.

In the 42nd STSC following recommendations were made on booster dose:

- Evidence from the CMC Vellore study suggest that when Covishield vaccine is given as booster, it gives a better immune response. However, the CWG may also review the data of protein sub-unit vaccines booster studies before a decision on mix-match booster could be taken
- There is no evidence on comparative value of precaution/booster dose at six months vs. nine months. Considering global evidence on six-month booster and no known safety concern booster dose may be administered at six months following last dose of primary series.

Vaccine Tracker Platform: There are three valuable databases present to monitor COVID-19 pandemic. (ICMR Lab data; MOHFW epidemiology and clinical data; CoWIN immunization data). Their harmonization will provide valuable policy and program relevant data on regular basis. ICMR informed that despite efforts, harmonization between CoWIN and the other database has not been possible. ICMR shared that it is not possible for them to extract this information. There is immediate need for mirror harmonization between all three national databases if these are to be value for decision making; this will be important for future relevance of these IT platforms as well.

In regard to people who were vaccinated from other parts of the world, following recommendations were made in the 32nd STSC:

- Partially immunized individuals: Priming doses should be completed by getting the second dose of the same vaccine if available in India
- If there is evidence of protection with mix and match for a particular pair of vaccines and one of the vaccines of that pair is locally available then that should be offered

- In all other situations, the priming may be completed by getting any of the available vaccines in India
- Precaution dose: may be completed with any of the available vaccines
- Those with complete immunization including booster(s) may be allowed to update their information on the CoWin Portal

Discussion

The chairperson once again thanked CWG and solicited, if there is a recommendation on mix-match for completing primary series, then is it possible to do mix and match for booster as well. It was clarified that mix-match recommendations for completing primary series and even boosters apply to specific group that had received partial or full primary vaccination from any other country and need to complete it primary series or need booster to get an adequate protection.

The chairperson, apprised about the three standalone databases: COVID-19 India portal, ICMR COVID-19 testing portal and CoWIN portal and sought guidance from Dr R S Sharma, CEO, NHA, for development of an amenable mechanism to harmonize these three databases. Furthermore, mechanism for updating vaccination records of Indian citizens who had received COVID-19 vaccine abroad in the CoWIN platform was requested.

Dr R S Sharma, shared the provision of updating records in CoWIN, for the people who received COVID-19 vaccine abroad is a software issue that can be facilitated in CoWIN for these special conditions. Furthermore, the harmonization of the three data bases has been a challenge as there are no common identifiers. If UID, would have been used as a common identifier then there would not have been any problem. Mobile number cannot be a common identifier as in CoWIN six people can get registered using one mobile number for vaccination. Here complete harmonization may not be possible but one can get partial results. In order to get harmonized data, common identifier need to be promoted across the three data bases. A team need to work on it NHA will provide support of technology team. The chairperson agreed with Dr R S Sharma and suggested formation of a team where nodal persons from ICMR and MoHFW may be also be included under the guidance of Dr R S Sharma. It will also help in making data available for research purpose.

It was also suggested that ABHA number could also be used by the three databases for future harmonization. ABHA ID can be generated on the spot and has already been generated for more than 10 million people. Members agreed that if the data could be linked to a common identifier across different disease databases, then it may be helpful for future research activities pertaining to different public health problems.

In reference to a query on immunocompromised definition it was shared that a list of immunocompromised conditions was shared as part of 36th STSC minutes.

Few members expressed concern over unavailability of immunogenicity data against Omicron infection. It was informed that there is some data on immunogenicity against Omicron is available it is lower when compared to original Wuhan strain to prevent infection. However, existing vaccines have worked well in

preventing severe disease, complications, hospitalization, need for ICU and ventilators and mortality. Attempt is being made around the world to develop multi-strain vaccines but that may take time.

It was mentioned that cellular immunity must be looked while considering a vaccine for prevention against severe disease instead of antibody levels. As of now all most whole population has been exposed to Delta or Omicron and had received primary series of COVID-19 vaccine. There is a case of hybrid immunity. Consideration of booster or multiple doses, may not be valuable if prevention of infection is looked at. If a person is given a vaccine of one particular antigen, sometimes giving another antigen may not be that valuable. Data on numbers of hospitalization, ICU admissions and deaths in different age groups may be looked proactively and data on co-morbid conditions may also be collected. It was suggested that routine testing of virus may be stopped and it should be done in hospital-based settings.

A member informed that the SWG-IVRCB had recommended several research studies on COVID-19 vaccine, some of the studies are ongoing, remaining studies may also be taken up.

Regarding the death data it was shared that there has been lot of reconciling in several states and information on specific data point couldn't be collected as required by the NTAGI. Revised testing strategy has been communicated in all districts. It is hospital based and if there is a rise in cases in a district then testing need to be ramped up. Samples are sent for genetic sequencing.

The chairperson and co-chairpersons suggested that STSC may consider discussion on feasibility of further booster and refining of testing strategy.

Recommendations

Based on the presentation and deliberations NTAGI endorsed the STSC recommendations on COVID-19 vaccines with following:

- The Standing Technical Sub-Committee may review the evidence on need for further booster in general population as well as special population groups.
- Evidence from CMC Vellore study suggest better immune response when Covishield is administered as booster. However, the STSC may also review the evidence from other recently concluded mix-match booster studies, including Corbevax booster study and submit its report for policy decision on mix-match boosters.
- Under the leadership of Dr R S Sharma, a team may be constituted to work on harmonization of COVID-19 India portal data, ICMR COVID-19 testing portal data and CoWIN data. Team will include one nodal person from ICMR and one from MoHFW. The NTAGI Secretariat may follow up with this newly constituted team and report the progress to STSC and NTAGI
- As per the list of immunocompromised conditions shared in the 36th STSC meeting, additional dose vaccination of immunocompromised people may be considered on priority basis

- Individual with partial or full vaccination history from abroad may be provided domestic available vaccines as per the recommendations of the 32nd STSC. These individuals may be allowed to upload their vaccine records in CoWIN portal.

The NTAGI will continuously review the new evidence on COVID-19 vaccines and SARS-CoV-2 variants epidemiology, and will revisit its recommendations every 3 months or earlier when deemed appropriate.

Agenda 5: NTAGI Work Plan, July-December 2022: Joint Secretary-RCH

Dr P Ashok Babu, Joint Secretary-RCH presented work plan for next six months. It included following activities:

Scientific Activities

Activity 1.1: Impact assessment of the COVID-19 Vaccines in different population groups-COVID-19 WG

Activity 1.2: Development of an IT mechanism to facilitate impact assessment of COVID-19 vaccines by using routine testing data, COVID-19 hospitalization and death data, sequencing data and COVID-19 vaccination data

Activity 1.3: Develop a report explaining the details of mechanism, methodologies, necessary systems, data points, manpower and support require for developing a platform/data warehouse which will in harmonizing data from various agencies, so that it can help in NTAGI work, as part of SWG-VPD Surveillance work

Activity 1.4: Review of the data of maternal seasonal influenza vaccination data in Maharashtra as part of Influenza working group work

Activity 1.5: A review of seasonal Influenza infection rates during pregnancy and its impact on maternal mortality, morbidity and fetal outcomes as part of maternal immunization sub-group work.

Activity 1.6: A brain storming workshop to discuss the issue of vaccine confidence with different stakeholders and subject matter experts as part of vaccine confidence sub-group work.

Activity 1.7: Guidance document on Typhoid surveillance following TCV introduction and impact assessment by NTAGI.

Activity 1.8: Formal documentation, and scientific publication of the experience of COVID-19 vaccine by COVID-19 WG

Strengthening of Technical & Scientific Capacities

Activity 2.1: Access to different Scientific Articles Databases for systematic literature review on VPDs

Activity 2.2: Capacity building of NTAGI Secretariat in following areas: Grade Evaluation, Health Economics, Disease Modeling.

Discussion

The Chairperson mentioned that activity 1.3 appears to be corollary of 1.2. It was suggested that the IHIP database may be refined based on the results of harmonizing three data bases of COVID-19.

It was suggested that research activities on COVID-19, HPV and JE may also be added as part of work plan.

Recommendation

- The NTAGI approved the work plan for next six month which included research activities pertaining to COVID-19, HPV and JE vaccines.

Concluding Remarks

The chairperson and co-chairperson expressed gratitude to all members and for their invaluable contribution to all five agenda items considered in the meeting. Discussions were extremely fruitful and beneficial. Based on these valuable discussions a decision on introduction of TCV and HPV vaccines in UIP has been made. With these remarks meeting was concluded.

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Annexure -1

List of Participants

S.No.	Name	Designation	Attendance
Chairperson			
1	Shri Rajesh Bhushan	Secretary, Department of Health & Family Welfare	In-Person
Co-Chairpersons			
2	Dr Balram Bhargava	Secretary, Department of Health Research & DG-ICMR	In-Person
3	Dr Rajesh S. Gokhale	Secretary, Department of Biotechnology	In-Person
Core Members, Ex-officio			
4	Dr Atul Goel	Director General of Health Services	In-Person
5	Ms Roli Singh	Additional Secretary & Mission Director, NHM	In-Person
6	Dr Sujeet Singh	Director, National Centre of Disease Control	In-Person
7	Dr Priya Abraham	Director, National Institute of Virology	Virtual
8	Dr Pramod Garg	Executive Director, THSTI, Faridabad	In-Person
9	Dr Pushkar Sharma	Director, National Institute of Immunology	In-Person
Core Members, Independent Experts			
10	Dr J P Muliyil	Professor, CMC Vellore	In-Person
11	Dr Gagandeep Kang	Professor, CMC, Vellore	In-Person
12	Dr Indrani Gupta	Professor, Institute for Economic Growth, Delhi	In-Person
13	Dr Rakesh Aggarwal	Director, JIPMER, Puducherry	In-Person
14	Dr Satinder Aneja	Former Director Professor, LHMC, New Delhi	In-Person
15	Dr Neerja Bhatla	Professor, AIIMS, New Delhi	In-Person
16	Dr Dilip Kumar Das	Professor, Burdwan Medical College, Burdwan	In-Person
17	Dr Parvaiz Koul	Professor, Sher-i-Kashmir IMS, Srinagar	In-Person
18	Dr F U Ahmed	Former Director NEIGHRIMS	In-Person
19	Dr N K Arora	Executive Director, INCLEN International	In-Person
20	Dr M D Gupte	Former Director, NIE, Chennai	Virtual
21	Dr Lalit Dar	Professor, AIIMS, New Delhi	Virtual
22	Dr Surinder Jaswal	Professor, Tata Institute of Social Sciences	Virtual
Liaison Members			
23	Dr P Ashok Babu	Joint Secretary-RCH, MoHFW	In-Person
24	Dr Veena Dhawan	Joint Commissioner-Immunization, MoHFW	In-Person
Professional Organization Representatives			
25	Dr Vineet K Saxena	President, Indian Association of Paediatrics	In-Person
26	Dr Sahajanand Prasad Singh	President, Indian Medical Association	In-Person
27	Dr K Srinath Reddy	President, Public Health Foundation of India	Virtual
International Partners Representatives			
28	Dr Payden	Country Representative, WHO, India	In-Person

29	Dr Luigi D'Aquino	Chief of Health, UNICEF	In-Person
State Representatives			
30	Dr Nivas	Andhra Pradesh	In-Person
31	Dr Nitin Ambadekar	Director Public Health Dept, Maharashtra	In-Person
32	Dr Kuldeep Singh Martolia	SEPIO, Uttarakhand	In-Person
33	Dr N K Sinha	SEPIO Bihar	In-Person
Special Invitees			
34	Dr R S Sharma	CEO, NHA	In-Person
35	Dr Alka Sharma	Scientist H, DBT	In-Person
36	Dr Pradeep Haldar	Former Advisor-RCH, MoHFW	In-Person
37	Dr Nivedita Gupta	Scientist F, ICMR	In-Person
38	Dr Jyoti Logani	Scientist F, DBT	In-Person
39	Dr Tanu Jain	Director, NCVBDC	In-Person
40	Dr Indu Grewal	Immunization Division	Virtual
41	Dr Ashish Chakraborty	Immunization Division	Virtual
42	Dr Shipra Verma	Immunization Division	In-Person
NTAGI Secretariat			
43	Dr Dinesh Paul	Advisor-cum-Manager	Virtual
44	Dr Awnish Kumar Singh	RA	In-Person
Member Apologized			
45	Dr Y K Gupta	Principle Adviser THSTI-DBT	
46	Dr Arun Kumar Agarwal	Professor, PGI, Chandigarh	
47	Dr Mathew Varghese	HoD, Orthopedics, St. Stephan's Hospital, New Delhi	
48	Dr V G Somani	DCGI, CDSCO	

Annexure-2

Agenda

Chair: Shri Rajesh Bhushan, Secretary (H&FW), MoHFW	***Co-Chair: Prof Balram Bhargava, Secretary DHR & DG-ICMR***	***Co-Chair: Dr Rajesh S. Gokhale, Secretary DBT***
11:00 AM-11:05 AM	General Business	NTAGI Secretariat
11:05 AM-11:10 AM	Welcome and Introduction Submission of minutes of the 16thNTAGI meeting held on May 28, 2021	Chair and Co-Chairs NTAGI
Agenda no. 1: Action Taken Report		
11:10 AM-11:15 AM	Agenda 1: Action taken report on the minutes of 16th meeting of NTAGI held on May 28, 2021	JS-RCH
11:15 AM-11:25 AM	Discussion	NTAGI Members
STSC Meeting Discussion and Recommendations		
Agenda no. 2: Typhoid Vaccines (Closed Session)		
11:25 AM-11:45 AM	Agenda 2: STSC discussion and recommendations on Typhoid	Chair, Typhoid WG
11:45 AM-12:00 PM	Discussion	NTAGI Members
Agenda no. 3: HPV Vaccines (Closed Session)		
12:00 AM-12:15 PM	Agenda 3: STSC discussion and recommendations on HPV	Chair, HPV WG
12:15 PM-12:25 PM	Discussion	NTAGI Members
Agenda no. 4: COVID-19 Vaccines (Closed Session)		
12:25 PM-12:35 PM	Agenda 4: STSC discussion and recommendations on COVID-19	Chair, COVID-19 WG
12:35 PM-12:45 PM	Discussion	NTAGI Members
Recommendations (Closed Session)		
12:45 PM-12:50 PM	Recommendations on the agenda item # 2-4 of the 17th NTAGI meeting	Chair and Co-Chairs NTAGI
Agenda no. 5: Work Plan of NTAGI 2022		
12:50 PM-12:55 PM	Agenda no. 6: Work Plan of NTAGI (July-December, 2022)	JS-RCH
12:55 PM-01:00 PM	Concluding Remarks	Chair and Co-Chairs NTAGI
01:00 PM-01:30 PM	***Lunch***	