Minutes of the meeting of the Core Committee on Vaccines

The Secretary (DHR) & Director General, ICMR had constituted a Core Committee on Vaccines under the Chairmanship of Prof. MK Bhan, Secretary, DBT, to examine the recommendations of Expert Group meetings on MMR and measles vaccine; Hepatitis B and Hib vaccines; JE vaccine and on vaccine production capacity to address specific questions the Secretary (Health) had posed and make recommendations to the Ministry of Health &FW on these vaccines and vaccine production potential for new vaccines. Two meetings (27th Jan and 26th April 2010) were held at ICMR headquarters. The list of participants is given below:

1. Prof. MK Bhan, Secretary, DBT (27th Jan, 26th April) - Chairperson
2. Dr. VM Katoch, Secretary DHR & DG ICMR (27th Jan, 26th April)
3. Dr. NK Sethi, Sr. Adviser , Planning Commission (27th Jan)
4. Dr. Shiv Lal, Special Director General Health Services (27th Jan)
5. Lt. Gen. D Raghunath, Bangalore (27th Jan)
6. Dr. RL Ichhpujani, Director, NCDC (26th April)
7. Dr. SD Khaparde, DC (Immn), MOHFW (27th Jan)
8. Dr. AC Dhariwal, DC (MCH), MOHFW (26th April)
9. Dr. Lalit Kant, Head (ECD), ICMR (27th Jan, 26th April)
10. Dr. Ambujam Nair Kapoor, ICMR (27th Jan, 26th April)

The Core Committee reviewed the recommendations of each of the Expert Committees. The minutes of the meetings of Expert Committee are appended to replies to questions.

The following is the summary of discussions and recommendations of the Core Committee.

I. Rubella

Issue:

Whether rubella is a public health problem in India necessitating introduction of rubella vaccine

Core Committee reviewed the minutes and recommendations of the Expert Committee on rubella and measles meeting held on 15th Jan.2010. The Core Committee noted that:

- The public health importance of rubella infection stems from the fact that rubella infection in pregnancy has the potential to cause Congenital Rubella Syndrome (CRS) in the new born. The risk of development of CRS is greatest when woman is infected in the first trimester of pregnancy.
- A number of serological studies of acquired rubella have been carried out. Overall recent cross sectional studies carried out since 1990, showed that a median of 16% (range 5-43%) (Ref.1-8) of women in reproductive age group are susceptible to rubella infection and are at risk of giving birth to children with CRS if exposed to rubella infection in pregnancy.
- Diagnosis of congenital rubella syndrome is difficult in young children. WHO estimates that 100 000 cases occur each year in developing countries. CRS is found in countries with high susceptibility rates among women of child bearing age (Weekly Epidemiological record 2000).
- Six studies from India have been included in international modeling study to estimate the CRS incidence in India. The average estimated incidence of CRS in India based on these studies was 123 per 100000 live births. (FT Cutts et al.,1999). Reported seronegativity for rubella in Pakistan was 16% in antenatal women, in Sri Lanka it was 43% (WHO Geneva 2000). Among the neighbouring countries Sri Lanka, Bhutan, Maldives and Thailand have introduced MR/MMR in their national immunization programme.
- A safe and effective vaccine exists since 1969 and administration of rubella vaccine would prevent occurrence of CRS. By the end of 2002, a total of 124 of the 214 countries/territories (58%) were using rubella vaccine in their routine immunization programme.

- Administration of rubella vaccine in childhood is the most feasible strategy. The risk is that this strategy requires very high routine immunization coverage as introduction of infant vaccination with inadequate coverage may decrease rubella virus circulation in children sufficiently with the resultant upward shift of the median age at infection; thus leading to higher proportion of girls remaining susceptible up to adulthood leading to a paradoxical increase in the number of rubella infections and of cases of CRS. Therefore introduction of rubella vaccine in UIP would require coverage of over 80%.

Conclusions & Recommendations

1. Available data shows that approximately 16 % of women in reproductive age group in India are susceptible to rubella. While there is no hard data on incidence of CRS, the estimated incidence from modeling is around 123 per 100000 live births. CRS gives rise to cumulative burden on the health system and to families of affected children on account of its chronic disability and the economic consequence for diagnosis, assessment and treatment of congenital malformations, challenges to providing education in an increasingly nuclear family structure. Given the severely disabling nature of CRS and enormous burden on poor families to sustain such children, application of safe and efficacious strategies is desirable.
2. Introduction of rubella vaccine as MR/MMR in the Universal immunization programme could be considered in states which have the ability to achieve and sustain routine immunization coverage of >80%. This would also provide a second opportunity for measles vaccination. Specific choice of MR/MMR should be made on the basis of incremental cost between the two. Mumps per se is not a significant problem.
3. Immunization of adolescent girls on a campaign mode with rubella vaccine or as part of adolescent health services under NRHM or in hospitals/private sector is recommended to offset the potential of increase of susceptible women in reproductive age group, if children alone are vaccinated.

4. Studies should be carried out to estimate incidence of CRS and the social and economic burden resulting from it.

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2. Measles

Issue: WHO appears to have stated that there should be two doses of measles vaccine administered rather than a single dose. Is this regimen being changed as the single dose is not efficacious or it is only to mop up those who missed it on the first dose? If the potency of one dose is good enough, why should the child be given twice and if not good enough, then we should cover all children?

- The estimated global measles deaths in 2007 were 197,000 of which India contributed about 67% (Weekly Epidemiological Record 2008). Majority of these deaths occur in states like UP, Bihar, Rajasthan, MP, Jharkhand and the North Eastern States.
- Measles vaccines are highly effective. Serum antibody response is used as evidence of protection from measles (i.e correlate of protection). Seroconversion rates vary depending on the age at immunization; seroconversion is better in children immunized at 12-15 months of age or older than at earlier ages.
- The average seroconversion rate with measles vaccination at 9 months is 85% (range 70-98%) (Job JS et al. 1984; Cutts FT et al.,1995). Approximately 15% of the children remain susceptible in spite of receiving one dose. The level of herd immunity needed to significantly impact measles transmission is in the range of 92-95% (Stanley Plotkins et al. 2008)
- Measles vaccine coverage in the country continues to be low. It is estimated that 8.5 million infants in India (36.5% of the infants worldwide) do not receive even the first dose of measles vaccine (Weekly Epidemiological Record 2008). Measles is a highly infectious disease requiring a high level of population immunity to induce herd immunity. In areas with low vaccine coverage the immunity gap is contributed by the large number of population that is unvaccinated. This leads to early accumulation of susceptible cohort and frequent outbreaks. These are also areas with weaker health systems. A second opportunity for immunization either through a campaign mode or if vaccination card exists, to those who did not receive the vaccine earlier would reduce the immunity gap.

- The WHO/UNICEF Joint statement on Global Plan for reducing measles mortality 2006-2010 recommends a second opportunity for measles immunization delivered either through routine immunization services or periodic supplementary immunization activities.

Conclusions & Recommendations

- Single dose of measles vaccine given at 9 months is effective in protecting 85% of infants vaccinated. Rationale for second dose is to achieve levels of protection (>92%) where reduction in transmission is achieved; further the second dose addresses the 15% non-responders at first immunization and in real life circumstances, allows an opportunity to reach those who have missed the initial immunization. It may be noted that there is wide acceptance of this view by all WHO member countries except India. Overall, based on these well established scientific facts, changing from one dose to 2 dose strategy would help catch up those missed but more importantly elevate the level of immunity to break transmission of disease.

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3. JE vaccination

Issue: "The reduction in morbidity and mortality on account of the vaccine programme can be assessed by looking at States like Andhra Pradesh where in last two years, after introduction of vaccine the morbidity and mortality seems to have become negligible in numbers. Is this due to the vaccine or improvement in sanitation etc. Should JE vaccine be introduced in the universal Immunization Programme."

Core Committee reviewed the minutes and recommendations of the Expert Committee meeting held on 27th Jan.2010. The Committee noted that:

- An estimated 3 billion persons live in countries where the JE virus is endemic, and the annual incidence of the disease is 30,000–50,000 cases (UN Report 2005). The disease can cause irreversible neurologic damage. The annual number of human deaths caused ranges between 10,000 and 15,000, and the estimated global impact from JE in 2002 was 709,000 disability- adjusted life years (DALYs) lost (Solomon 2006; WHO Report, 2008). Approximately 45-50% of surviving patients exhibit serious residual neurological disability (Japanese Encephalitis.p.315. Stanley Plotkins et al. Vaccines: Fifth Edition).
- In India there are 135 JE endemic districts. Maximum JE cases occur in UP and Assam. A study carried out in South India showed JE incidence to be 15/10,000 among the children between 5-9 years (Gajanan et al, 1995). Mortality due to JE has been estimated to be between 20-30% (Barhua HC, et al, 2002, Dhillon et al., 2008). Recent studies under the WHO surveillance program in India undertaken in selected centers (Bellary, Dibrugarh, Madurai and Burdwan) in last two years show that about 10-20% of the total Acute Encephalitis Syndrome (AES) cases are due to JE. Data from WHO surveillance suggests that there is no change in AES cases from 2007 to 2009 in areas where surveillance is ongoing (Personal Communication. V.Ravi). A

recent study showed one third of the cases affected in India had neurological sequelae one year after infection (Baruah et al. 2002).

- Till 2005, all AES cases were being labelled as JE. After 2005, aetiological diagnosis of AES for JE is being established to some extent. After immunization programme was introduced, only JE confirmed cases are being reported. There is no baseline data on JE confirmed cases prior to introduction of vaccine. Hence it is not possible to conclude confidently that the decrease is due to vaccination or other interventions or the other way around. In 2005, test for Chandipura became available, positive cases from these tests was being labeled as Chandipura. Also, JE has a cyclicity of 4 years. In view of this it is difficult to assess trends in JE.
- Of all the AES cases that occur it is estimated that about 20% are due to JE, 4-5% are due to bacterial infections, 1-2% are due to enterovirus infection and for the remaining the cause is not established (NIV Unpublished data from Gorkahpur area). However, AES is now known from global experience to be caused by a variety of different microorganisms.
- Environmental management for vector control, chemical control of vector populations, immunization of pigs or keeping them in a mosquito proof enclosure are not feasible in India .Virus circulation cannot be stopped and therefore, immunization is the mainstay for prevention of JE. JE has been controlled in other countries mainly on the basis of effective vaccination programmes, mechanized farming practices and overall improvement in the life style.

JE Vaccine Immunogenicity and Protective Efficacy

- In India, one dose of SA-14-14-2 imported from China is being used in the programme. A neutralization antibody titre of more than 1:10 is generally accepted as evidence of protection and post vaccination seroconversion. SA-14-14-2 has been found to be effective in a single dose preventive campaign followed by routine administration to infants in reducing public health burden of JE (Bista MB et al, 2000).
- The protective efficacy of a single dose of SA-14-14-2 JE vaccine 12 to 15 months after administration of vaccine in Nepal was 98.5% (CI: 90.1-99.2%) (Ohrr et al,

2005); this efficacy was maintained at 96.2% at five year follow up (Tandan JB et al., 2007). Achievement of a sustained reduction in JE in areas where many children received only a single dose of SA-14-14-2 vaccine, suggests that the efficacy of this vaccine exceeds the ability to detect a circulating neutralizing antibody response to a single administered dose.

- Data from post marketing surveillance (PMS) in India (ICMR unpublished study) showed that protective efficacy of the vaccine in India is not as high as that seen in Nepal. PMS study showed that virus neutralizing antibodies were seen in 45.7% of children before vaccination. Sero-conversion against Indian strains 28 days after vaccination was 73.9% and 67.2% in all individuals and in those who were non-immune pre-vaccination respectively. The protective efficacy of the vaccine at one year was 43.1% overall and 35% for those who were non-immune pre-vaccination respectively.
- Preliminary results of a case control study carried out by ICMR on impact of JE vaccine shows an unadjusted protective effect of 62.5% in those with any report of vaccination.

Vaccine Coverage

- Independent evaluation of vaccine coverage shows that vaccine coverages in the programme were very low. UNICEF coverage report shows a big difference between reported and evaluated coverage figures e.g, In Dibrugarh it was 90.5% vs. 35.9% and Gorakhpur 97% vs.52.3 % for reported and evaluated coverages respectively.

Conclusions & Recommendations

- It is difficult to comment on whether reduction in JE cases is due to improved sanitation etc. rather than immunization as no baseline data are available prior to immunization.
- The only effective strategy for control of JE is vaccination. In endemic areas, the WHO recommends a one time catch up campaign followed by incorporation of JE vaccine into routine immunization programme. (WHO Position Paper. Weekly Epidemiologic Record 2006). Mortality and disability in India due to JE is high. Evaluated coverage of campaigns already implemented is lower than reported coverages in most states evaluated. Therefore, it is recommended that all children

aged one year to 15 years be immunized irrespective of previous reported immunization status in a campaign mode in 2010 ensuring good vaccine coverage. Thereafter, immunization of children less than 2 years may be sustained through routine immunization. The existing JE surveillance systems should be effectively strengthened to allow a reliable estimation of immunization impact.

- A study preferably in Assam (surveillance is good, there is an ICMR centre, baseline data is available in Dibrugarh) should be carried out to examine the impact of 2 doses vs. single of SA-14-14-2 vaccine.

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4. Hepatitis B

Issue: Hepatitis B spreads through both horizontal and vertical transmission. Whether there are other strategies available to identify key target groups to be given Hep.B vaccines rather than introducing for universal application even among low risk and no risk children

The Core Committee carefully examined the different view points on the issues among members of the Expert Group and offered specific recommendations. These views are summarized in the minutes. The Committee noted that:

- A representative sample of pregnant women is considered to adequately reflect the status of normal population. Data from studies in pregnant women show that HBV carrier frequency among pregnant women is about 3%. In a meta-analysis of prevalence of Hep.B in India, the prevalence of HBV was 2.4% in non-tribal population. Higher figures have been reported in (15.9%) tribal population (Ashish B et al. 2007). From published data in pregnant women and population based studies, the HBV carrier rate in India can be considered as at least 2 to 3 % indicating that about 20 to 30 million chronically infected HBV persons exist in India.
- In India, a study carried on HBV transmission by Nayak et al (1987) showed that on the whole, 75% of HBV carrier acquires infection by horizontal spread before 5 yrs. of age and presumably 25% by vertical transmission.
- There is no registry for Hepatitis B in India till date. Information on incidence of hepatocellular carcinoma (HCC) is primarily derived from the ICMR Cancer Registry programme. The projected cases of HCC from ICMR cancer registry in 2009 was 22238 cases.
- There are 8 genotypes of HBV. The HBV genotypes prevalent in India are D in 60-70%, A -20-30% and C approximately 5% (mainly from East India). There is

evidence that the duration of the hepatitis B e-antigen (HBeAg) positive replicative phase varies for the different genotypes, being shorter for A&D which dominate in Africa, the Mediterranian region, the Middle East, and India, than for B and C which dominate in South East and East Asia; this is the reason for vertical transmission being common in the latter countries than in the former ((Norder et al 2004). An ICMR study in tribal areas of Orissa and MP showed the prevalence of HBV to be between 1 and 5% and genotype D being the predominant genotype associated with chronicity and morbidity (DHR Annual report 2009-2010).

- Long term consequences of HBV infection depend on the chronicity of infection which in turn depends on the age at acquisition of infection – the younger the age at infection, the greater is the likelihood of development of chronicity. HBV acquired early in life results in cirrhosis, liver failure or HCC in upto 40% of individuals (N Engl J Med 2002). In patients with liver disease HBsAg positivity is seen in 12.5 – 21% of Acute viral hepatitis, 11-27% of acute liver failure, 40% of sub acute hepatic failure , 40-60% of chronic liver disease and 60-80% of hepatocellular carcinoma (Different studies summarized in S.K. Acharya et al 2006).
- The cost of treating these patients is prohibitive. One estimate from AIIMS researchers is that the estimated cost of treating chronic liver disease patients in India is Rs 12- 14 billion per year and at least one lakh deaths occur per year due to cirrhosis and HCC. A cost effectiveness study has shown universal immunization to be highly cost effective. Universal immunization reduced the HBV carrier rate by 71% and increased the number of years and QALY lived by a birth cohort by 0.173 years and 0.123 years respectively (Rakesh Aggarwal et al 2003).
- Majority of infected children have mothers not infected with HBV. 30% of HBV infections do not have an identified risk, less than 25% heterosexuals can identify the source. Based on the evidence that HBV infection in childhood occurs mostly by horizontal transmission in India (Nayak et al 1987), selective immunization will prevent only approximately 15% of HBV carriers while Universal Immunization will prevent upto 95% of HBV carrier state.
- Selective vaccination of children of well characterized pregnant women will not prevent the disease transmission that is mostly occurring horizontally. The cost of

screening followed by vaccination is greater than the cost of universal vaccination and impractical where antenatal care and hospital delivery are unassured. Thus the approach of screening followed by vaccination will not prevent a substantial part of even the vertical transmission

- A birth dose is essential to prevent vertical transmission, it will prevent vertical, horizontal transmission and should be given for all institutional deliveries and in other areas where feasible.
- At current institutional delivery rate of 47% (DLHS-3 (2007-08)), the institutional delivery rates have increased to 47% (2007-08) from 40 % in DLHS -2 (2002-04); with inputs under the NRHM this rate is expected to increase even further. This shows that the most ideal immunization regimen starting with a birth dose can be accessed by 10-12 million children of our annual birth cohorts.

Conclusions & Recommendation

- To be maximally beneficial, the immunization schedule should begin at birth; a birth dose of Hep.B vaccine should be given in all institutional deliveries.
- Given that available evidence suggests that the Hepatitis B prevalence in India is at least 2% and that horizontal transmission is important and given the serious health consequences in terms of chronic liver diseases and cancer and the social and economic burden of the affected, Universal immunization with Hepatitis B vaccine is recommended with immunization starting at birth for all institutional deliveries or others where feasible and with EPI schedule for all infants. The consensus was that immunization be initially taken up in some states, depending on availability of resources.
- Impact assessment on carrier rate should be part of ongoing programme. A framework for measuring impact should be made
- Roll out to other states would be guided by ongoing experience and impact assessment.

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5. Hib and Pentavalent vaccine

Issue: There is a proposal to introduce pentavalent vaccine that includes DPT, Hep.B and Hib. Is there adequate evidence about public health importance of Hib in the country? If so, is there a need for pentavalent vaccine?

The Core Committee had discussed in detail, the pros and cons of introducing Hib vaccine. Both points of view summarized in the minutes of Expert Group were discussed. The Core Committee noted that:

- Pyogenic meningitis cases are commonly seen in pediatric wards and constitute 2-4% of all pediatric admissions. Most of the children affected are less than 2 years of age. The two most common causes of pyogenic meningitis is *Haemophilus influenzae b* (Hib) and *Streptococcus pneumoniae*. Of the children with pyogenic meningitis, a third each of cases die, recover with sequelae or recover fully.
- Hospital based studies (8 studies) show that a median of 17% of probable meningitis (based on csf cell count, and/or elevated protein or decreased glucose (range: 9-35%). A median of 39% (range: 29-88%) of etiologically characterized meningitis cases confirmed by culture or identification of a bacterial pathogen (5 studies) are due to Hib. Mortality due to Hib meningitis has been observed to range from 13 to 67%. There has been no major change in these rates over the years. Age groups most affected are children less than two years. Antibiotic use prior to LP is high and is the cause for low sensitivity to culture and gram stain
- Overall available evidence from hospital based studies in India shows Hib to be an important cause of bacterial meningitis and pneumonia. The estimates above are likely underestimates as all children with disease reach hospitals late or after antibiotics have been consumed.
- In another study of the ICMR study (Part A- site preparation for a vaccine probe study) showed an incidence of severe pneumonia ranging from 2717 to 7890 per 100,000 child years of observation and suspected meningitis ranged from 1971 to 2433 per 100,000 child years of observation. In the hospital based study arm, a total

of 269 physician diagnosed meningitis, 7.9%, 29.6% and 21.0% of csf samples with cell count more ≥ 100 WBCs/mm^3 were purulent . Of these purulent meningitis 16.7%, 22.7% and 29% were Hib positive by culture or antigen at Chandigarh, Kolkatta and Vellore respectively, considering all sites together 24% of purulent meningitis were Hib. Nasopharyngeal carriage rate varied from 6 to 7.6% across the three sites.

- The above estimates have remained generally stable over a long period of time ranging from 1976 to 2009.
- A population based study on incidence of Hib meningitis in India (Minz.et al) showed an incidence of Hib meningitis of 7.1 per 100,000 children under 5 years of age, 19 per 100,000 children in children less than 2 years of age and 32 per 100,000 infants (Minz et al. 2008)
- Data on disease surveillance in Kerala for 1999-2000 (John et al. 2004) showed 75 meningitis cases of which at least 27 were bacterial meningitis. Assuming that one third of this is due to Hib, for a 26 million birth cohort, the estimated Hib meningitis is 52000 per year. Using the validated Hib Rapid Assessment Tool estimates, that allows pneumonia burden estimates based on meningitis data, the estimated Hib pneumonia cases would be 260000 per year (WHO 2001).
- A study on the community effect of Hib vaccination carried out in Vellore (Verghese VP et al. 2009), showed that for less than 4500 infants immunized, 7 cases of Hib meningitis was prevented which work out to approximately 166 per 100000 infants and 33 per 100000 under five children immunized per year.
- Pyogenic meningitis is a medical emergency to be diagnosed and treated within 8 hours. Health care system is unable to provide prompt, equitable health care and rehabilitation of assured quality to rural, peri-urban and urban poor. Hence prevention is ethical. It has been demonstrated that Hib vaccine is associated with high herd immunity and therefore greater levels of population level protection, effective even when immunization coverage is 50%.
- Reported association of Type 1 diabetes and Hib vaccination has been a concern highlighted by some but this has not been corroborated by any of the other studies reported around the world.

Vaccine Formulation

- The choice of vaccine formulation must take into account the requirements for cold chain cost and the child's comfort with regard to number of injections required. The pentavalent vaccine offers advantages of overcoming additional cold chain requirements and reduces the number of injections required per child.
- In Western countries pentavalent or hexavalent vaccine is used (Those who do not use Hep.B use IPV). Pentavalent vaccine is also used by our neighbouring countries. Reports of serious adverse events from Sri Lanka with pentavalent vaccine have been investigated and there were no serious adverse events related to the vaccine. Sri Lanka has resumed immunization with Pentavalent vaccine since 1st March 2010. Pakistan has administered 16,473, 897 doses of pentavalent vaccine; the coverage was 88%. There have been no reports of adverse reactions. But at the beginning of introduction there was one death; investigation by EPI as well as WHO found it to be unrelated to the immunization. Bhutan had introduced Pentavalent vaccine; but following 4 deaths after introduction of vaccine the government has suspended use of pentavalent vaccine pending investigation.

Summary and Recommendations:

- Hib is a major cause of pyogenic meningitis and severe pneumonia in children in India. Conservative estimates from available data in India on disease burden suggest that 52000 cases of meningitis and 260000 cases of pneumonia occur every year due to Hib.
- In Child Health Programmes the contribution of pneumonia to under five mortality remains to be 20% despite major efforts indicating relative difficulties of case management. Therefore, preventive strategies are important where efficacious vaccines are available.
- Hib vaccine is highly efficacious and at modest coverage of target population it gives high herd immunity.
- In view of the above consideration, Hib containing pentavalent vaccine is recommended to be introduced in some states depending on fund availability.

- To complement the data from etiology studies, the introduction of Hib vaccine should be used to gain insights into the impact of initial vaccine introduction on a sufficient sample size using the most feasible methods determined by an expert group.
- Roll out to other states can be guided by experience from first phase of introduction and by the impact assessment of the vaccine within the initial programme.

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5. Vaccine Production

Issue: "Whether our laboratories can produce DPT+ Hep.B vaccine and JE vaccine as then these vaccines would be available from them at cheaper rate"

The Core Committee discussed the observations of the Expert Group meeting on Vaccine production and noted the following:

1. DTP-Hep.B

a. As of December 2009, no public sector vaccine manufacturing units, were producing (DPT+Hep.B) combination vaccine in India. CRI, Kasauli which would have an installed capacity of 40 million doses of DPT, can procure and blend it with Hep.B and bottle it for use in India. Pasteur Institute, Coonoor can make upto 40 million dose of DPT, there is a proposal to produce Hep.B also in future.
b. In private sector Biological E (produces individual and Combination DPT – 80m; and Hep.B 20 m); Panacea (produces DPT+Hep.B and is WHO pre-qualified); Bharat Biotech (combo DPT+ Hep.B) 20 md/year; and Shanta Biotechnics (comb DPT+Hep.B) produce the DPT + Hep B vaccines

2. JE

a. Public Sector: CRI Kasauli used to produce 5 lakh doses of mouse brain derived JE vaccine (not used anymore as given in 3 doses), Pasteur Institute Coonoor can also produce, training of staff has been completed. BIBCOL can also produce but does not have infrastructure
b. Private Sector: Panacea working with Indian strain provided by NII, proposed time line of 18 months, installed capacity of 20 md /yr (in vero cell); Biological E – SA-14-14-w derived JE vaccine, capacity 20md/yr; Bharat Biotech working with Indian strain provided by NIV, awaiting DCGI approval for clinical trials, 50 million doses of vero cell vaccine

Recommendations

- Encourage public sector investment in combination vaccines (Quadrivalent + Hib separately; or pentavalent) to ensure affordability and vaccine security for the masses. It is necessary to ensure quality of vaccines. Among existing vaccines, for DPT and Hep.B, it is relatively easy to monitor good quality, because antibody is a good marker of protection. For other vaccines, Government may consider commissioning specific institutes with expertise to standardize given vaccine.

  One way to ensure sufficient quality in public sector is to standardize pilot lot production and transfer to a public sector company. Suitable institutional framework should be developed.
- The minimum standard for vaccine quality should be WHO pre-qualification
- A potentially effective strategy is to develop an approved generic technology and then license it out to different public sector companies.