Summary of Key Points

WHO Position Paper on Vaccines against Japanese Encephalitis (JE)
February 2015
Japanese Encephalitis Virus (JEV) is the leading cause of viral encephalitis in Asia
- Infection is common, but severe disease is rare (~1/250 infections)
- Transmitted by *Culex* mosquitoes; circulates in pigs and wading birds
- Predominantly affects South East Asia and Western Pacific Regions

Approximately 68,000 severe clinical cases of JE estimated to occur each year
- 20-30% case fatality rate
- 30-50% of those who survive can have permanent neurologic or psychiatric sequelae
- Children traditionally at greatest risk, but JE can occur in all ages
- No specific antiviral treatment for JE
Vaccines

- Four broad classes of JE vaccines currently in use:
  - Inactivated Vero cell-derived vaccines
  - Live attenuated vaccines
  - Live recombinant vaccines
  - Inactivated mouse brain-derived vaccines

- Assessment of the population impact of vaccination programs show when high coverage is achieved and sustained in populations at risk of disease, JE in humans can be virtually eliminated
Inactivated Vero cell-derived vaccines

- **Immunogenicity/effectiveness:**
  - Studies of one vaccine in non-endemic settings show high seroprotection rates after vaccination, but a possible decline in the 24 months following primary immunization.
  - High seroprotection rates demonstrated in among children in endemic settings, with high seroprotection rates up to 3 years post-primary series in one small study.
  - There are currently no vaccine effectiveness data from use in endemic settings.

- **Safety:**
  - Acceptable safety profile based on clinical trial data and the available post-marketing data.
Live attenuated vaccines

- **Immunogenicity/effectiveness:**
  - Studies show high post-vaccination seroprotection rates among children in endemic settings following a single dose
  - Good vaccine effectiveness (VE) was demonstrated in children vaccinated in a mass campaign
    - VE 99.3% 1 week-1 month post-vaccination
    - VE 98.5% 1 year post-vaccination
    - VE 96.2% 5 years post-vaccination

- **Safety:**
  - Acceptable safety profile based on clinical trial data and a large post-marketing database
Live recombinant vaccines

- **Immunogenicity/effectiveness:**
  - Studies show high seroprotection rates following a single dose in children in endemic settings and adults in non-endemic settings
  - Longer-term follow up from trials is limited but the majority of participants had seroprotective antibody titers 5 years after a single dose
  - There are currently no vaccine effectiveness data from use in endemic settings

- **Safety:**
  - Acceptable safety profile based on clinical trial data and the available post-marketing data
WHO Position

- JE vaccination should be integrated into national immunization schedules in all areas where JE is recognized as a public health priority

- High vaccination coverage should be achieved and sustained in at-risk populations

- Recommended strategy:
  - One time campaign in primary target population (typically <15 years of age), followed by incorporation into routine childhood immunization program
  - Older groups should be considered for vaccination if disease burden is sufficiently high
WHO Position

- Inactivated mouse brain-derived vaccines should be replaced by the newer generation JE vaccines
  - Inactivated mouse brain-derived vaccines may continue to play a role in some countries
  - However, overall they have a less favourable safety profile, variable manufacturing and cost, and require higher number of doses, and boosters

- Co-administration with other vaccines
  - Despite a lack of comprehensive immunogenicity/effectiveness and safety data for all possible combinations of JE and other routine vaccines, co-administration for programmatic reasons seems acceptable
Recommended vaccine dosing schedules

- Inactivated Vero cell-derived vaccine:
  - Manufacturer’s recommendations, which vary by product
  - In general, 2 doses at 4-week intervals, starting at ≥6 months of age in endemic settings

- Live attenuated vaccine:
  - Single dose at ≥8 months of age

- Live recombinant vaccine:
  - Single dose at ≥9 months of age

- Need for booster dose in endemic settings has not yet been clearly established for any of the listed vaccines
WHO Position

- Immunocompromised persons (including HIV-infected individuals):
  - Inactivated JE vaccine use is acceptable and preferential over live vaccines
  - HIV testing is not a prerequisite for vaccination
  - Immune response to vaccines may be lower compared to immunocompetent persons

- Pregnant and lactating women:
  - Vaccine may be given in case of sufficiently high risk of JE
  - Inactivated is preferred over live vaccines, as a general precaution
  - Pregnancy testing is not a prerequisite for vaccination
  - Inadvertent administration of live vaccine is not an indication for termination of pregnancy
WHO Position

- **Health care workers:**
  - Those in high risk endemic areas (e.g. involved in vector control) should be vaccinated

- **Travellers:**
  - Vaccine recommended for those traveling to endemic areas with extensive outdoor exposure during transmission season or migrating to JE-endemic areas
  - Vaccine schedule
    - Same recommended dosing schedule as for endemic population
    - Booster dose of inactivated Vero cell-derived vaccine may be given at >1 year after primary schedule if at risk for further exposure
    - Additional data are needed to inform recommendations for booster doses in child travellers
WHO Position

● Surveillance:
  – All JE-endemic countries are encouraged to carry out at least sentinel surveillance with laboratory confirmation of JE
  – While a comprehensive JE surveillance system is recommended, countries without a strong system in place but with evidence of JE disease should not wait to introduce JE vaccine

● Research priorities:
  – Data on long-term immunogenicity, vaccine effectiveness, and vaccine impact
  – Specific data on specific vaccines in specific populations
    • E.g. long term data in young child travellers, immunogenicity and safety of live attenuated vaccine in adults
  – Development of standardized neutralization assay reagents and sensitive, specific, affordable commercial serological reagents to ensure access to diagnostic testing in JE-endemic countries
For more information on the WHO JE position paper, please visit the WHO website:

www.who.int/immunization/documents/positionpapers