# Summary of Key Points

# WHO Position Paper on Vaccines against Japanese Encephalitis (JE) February 2015

World Health Organization

# Background

- 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

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