



Report to the GAVI Alliance Board

21-22 November 2013

Subject:	Consent Agenda: Opening of Funding Window for Japanese Encephalitis
Report of:	Hind Khatib-Othman, Managing Director, Country Programmes
Authored by:	Stefano Malvoti, Director, Vaccine Implementation, Tania Cernuschi, Senior Programme Manager, Johanna Fihman, Programme Manager
Agenda item:	02h
Category:	For Decision
Strategic goal:	SG1 - Underused and new vaccines

Section A Overview

1 Purpose of the report

- 1.1 The purpose of this report is to request the Board to open a funding window for Japanese Encephalitis (JE) vaccines.

2 Executive Summary – Update

- 2.1 Following the November 2011 Board decision, the Secretariat together with partners have initiated the programme design to enable opening a window for JE in 2014 once WHO prequalification for the JE vaccine was given.
- 2.2 The WHO prequalification of a JE vaccine was announced on 9 October 2013.

3 Recommendations

- 3.1 At its meeting on 9-10 October, the Programme and Policy Committee recommended to the GAVI Alliance Board that it:

Open a funding window for JE vaccine such that the GAVI Secretariat can invite country proposals for support in 2014 from all GAVI eligible countries at risk.

4 Risk and Financial Implications – Update

- 4.1 In accordance with GAVI's policy, operational costs will be covered by GAVI for JE campaigns in GAVI eligible countries. The total expenditure



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for the period 2015-2020 is expected to amount to US\$ 105M¹. This is included in the current financial forecast.

4.2 Risks linked to the JE window are addressed in the PPC paper (attached).

¹ GAVI will also pay for the vaccine cost, syringe and safety box, and shipment costs. Countries will then fully fund routine programme and will receive the Vaccine Introduction Grant from GAVI.



Report to the Programme and Policy Committee

9-10 October 2013

Subject:	Country Programme Update: Japanese Encephalitis
Report of:	Hind Khatib-Othman, Managing Director, Country Programmes
Authored by:	Stefano Malvoti, Director, Vaccine Implementation and Johanna Fihman, Programme Manager, Vaccine Implementation
Agenda item:	04b
Category:	For Decision
Strategic goal:	SG1 - Underused and new vaccines

Section A: Overview

1 Purpose of the report

- 1.1 This report requests the PPC to endorse a decision to open a window for Japanese Encephalitis (JE).

2 Recommendations

- 2.1 The PPC is requested to

Recommend to the GAVI Alliance Board that it opens, a funding window for JE vaccine subject to the Secretariat receiving confirmation of WHO prequalification of a vaccine such that the GAVI Secretariat can invite country proposals for support in 2014 from all GAVI eligible countries at risk.

3 Executive summary

- 3.1 The prequalification of a Japanese Encephalitis (JE) vaccine for paediatric use is imminent. As a result and based on the November 2011 Board decision, the Secretariat together with partners has initiated work that would enable opening a window for JE in 2014.
- 3.2 While the overall implementation strategies remain unchanged from those presented to the PPC in 2011 (see Annex A), Nepal and Vietnam have been added to the list of countries eligible for JE support. They have a history of self-funding JE programmes (campaigns and routine) in some but not all parts of the country. They should be considered eligible for GAVI support for their currently unreached population at risk.

- 3.3 In addition, new surveillance data may become available in different countries in the region which will allow better assessment of the population at risk. Some countries¹ have already initiated JE vaccination programmes in some areas – routine or campaigns. While most of the countries are targeting the entire population, a limited number of them are foreseen to require support only for a portion of the population. For those countries a change in the epidemiology may result in variations of financial needs and impact estimates. The assessment of countries' target population for GAVI support will thus be a key element and will be requested in countries applications.
- 3.4 The WHO position paper for JE will be revised in 2014. The Secretariat will be following closely the evolution of the discussion to ensure GAVI support is in line with WHO's recommendations. An update will be provided to the PPC should major changes occur.
- 3.5 JE is already included in the financial forecast for the balance of demand for 2014 and 2015.

4 Risk implication and mitigation

- 4.1 JE campaigns must be conducted in the first or last quarter of the year due to the rainy season. Should the announcement of the JE vaccine's prequalification be delayed to 2014, it is not clear that sufficient time will be left to allow countries to conduct campaigns in 2015². First introductions would then be delayed to late 2015 or 2016.
- 4.2 WHO will be revising the JE position paper in the coming months. The Working Group is expected to present its recommendations to SAGE in October 2014 including new data on schedules, duration of protection and co-administration. It is worth noting that although WHO considers that one dose of the SA14-14-2 can induce significant long-term protection (up to 11 years)³, some countries such as India recommend a two dose schedule. Changes in the WHO recommendation on the JE vaccine schedule would raise the question on the affordability and sustainability of JE routine programmes currently assumed to be fully financed by the countries. An update will be provided to the PPC when available.
- 4.3 Although JE is a priority in Asia, it will be competing with other vaccines recent or future introductions. Countries are likely to need additional support in their decision making process and to effectively prepare for the integration of an additional vaccine in their immunisation programme.

¹ Lao PDR, Cambodia, Korea PDR.

² At least two countries – Cambodia and Lao PDR – are ready to apply for GAVI support as soon as the window opens and will be willing to plan campaigns as soon as possible.

³ Based on the 2006 WHO position paper.

5 Financial implications: Business plan and budgets

- 5.1 JE is already included in the financial forecast for the balance of demand for 2015. As described above, adjustments to target population may lead to variations to countries' specific approvals. Based on history of JE programmes and current assumptions on the population at risk in these two countries, the addition of Nepal and Vietnam to the list of eligible countries for GAVI support will not require a significant increase to the current budget. In 2014, GAVI will focus on SDF v9.0 to have more precision on countries plan and provide a long term perspective on financial requirements.
- 5.2 JE is currently included in the Business Plan with other new vaccines to support countries decision making and preparation for applications. The need for additional budget for surveillance is currently included for consideration in the 2014 Business Plan.

Section B: Content

6 Programme design considerations

- 6.1 In 2011 the GAVI Board decided to open a window for applications once an appropriate JE vaccine is pre-qualified. The live attenuated SA 14-14-2 vaccine is expected to receive WHO pre-qualification imminently. This vaccine was developed by Chengdu Institute of Biological Products (CIDBP) with support from PATH and is expected to be available in sufficient quantities to meet GAVI demand.
- 6.2 The programme implementation strategies remain unchanged (see Annex A Japanese Encephalitis Implementation Strategy presented to the PPC in September 2011). GAVI will fund catch up campaigns for 9 months to 15 year olds: GAVI will pay for the vaccine cost, syringe and safety box, and shipment costs. Countries will then fully fund routine programme and will receive the Vaccine Introduction Grant from GAVI.
- 6.3 Due to the seasonality of the disease⁴ and the logistical complexities during the rainy season, campaigns should be conducted in the first or last quarter of the year. With support from partners and providing the prequalification of a JE vaccine is announced by end of 2013, GAVI will develop application guidelines in time for countries to apply in 2014 allowing for first campaigns in the first quarter of 2015.
- 6.4 Out of the eight endemic countries eligible in 2011, two will be on the graduation path in 2014⁵. As described above, the PPC is asked to endorse the addition of Nepal and Vietnam as eligible countries for GAVI support. Nepal has conducted JE vaccination campaigns in all 31 endemic

⁴ In most temperate areas, JE is transmitted mainly during the warm season, when large epidemics occur. In tropics and sub-tropics, transmission can occur year-round but often intensifies during the rainy season.

⁵ Timor Leste and Papua New Guinea will be graduating from GAVI support in 2014.

districts based on JE surveillance data (2004-2005). Based on on-going surveillance of JE disease, Nepal may apply for GAVI support in the future if any of the remaining districts are found to be at risk of JE. In Vietnam, since 1997, children up to five years of age are vaccinated in 596 of the 696 districts with a mouse brain locally produced vaccine. 80% of the country's target population of children under five years old has already been reached with vaccination. Even though it is unlikely that Vietnam would at this stage switch to the live SA14-14-2 vaccine, there are gaps in the remaining 20% of the country's target population and children up to 15 years old of age in areas where under five vaccination was recently initiated. In addition, experience in Sri Lanka shows that the two vaccines can be combined⁶. Boosting children previously vaccinated with inactivated vaccine could provide a longer duration of immunity and acceleration of JE control. Vietnam could thus apply for campaigns to reach the 20% and catch-up campaigns to reach the additional children up to 15 years of age.

- 6.5 Overall, even though the JE surveillance has improved, increased awareness of disease burden at the national and regional levels are required. The definition of the target population for JE will be challenging due to the lack of data but also to history of past campaigns conducted in some countries such as Lao PDR, Cambodia and Korea PDR. This may lead to changes in the financial forecast. As part of their application for GAVI support, countries will be asked to provide an assessment of the target population. Additional surveillance data will be needed to better assess population at risk.
- 6.6 The programme cost estimates have been revised to reflect changes in countries eligibility based on the Strategic Demand Forecast including latest information received from countries. It is currently estimated that GAVI will disburse US\$ 91 million between 2015 and 2020 to support campaigns in the six eligible countries at risk to reach over 68M children under 15 years of age. Further data will be required to assess potential support to Nepal and Vietnam.

Section C: Implications

7 Impact on countries

- 7.1 Recent improvement in surveillance with better understanding of the burden and geographical extent of disease has resulted in greater recognition of JE as a public health problem. The opening of this new window will allow GAVI to catalyse vaccine uptake in the region.
- 7.2 JE is an inexpensive vaccine – estimated to cost around 40 cents per dose. To increase country ownership and sustainability, countries will

⁶ A publication is being prepared on the experience that immunity gained through the mouse brain-derived inactivated vaccine could be boosted with a subsequent dose of live attenuated vaccine.

receive full support for campaigns and will be asked to pay for routine introduction.

8 Impact on GAVI stakeholders

8.1 Surveillance is crucial to better understand vaccine efficacy and measure impact. GAVI stakeholders will need to continue efforts to strengthen surveillance programmes in JE endemic countries.

8.2 JE is a time-limited project with a regional focus. It provides the Alliance an opportunity for an in-depth assessment of programme design processes. The Secretariat and partners could develop a tailored approach to design the programme appropriately to meet the needs of all eligible countries at risk. This would provide valuable learning for future GAVI windows.

9 Impact on Secretariat

9.1 There is currently no dedicated position for JE. The workload generated by the programme will need to be incorporated into the existing Vaccine Implementation team structure. Consequently, the focus will remain on high level programme management unlike other new programmes such as HPV or IPV.

10 Legal and governance implications

10.1 Once a window is open for JE vaccines, grant arrangements will be made with countries for approved proposals in line with existing GAVI arrangements.

11 Consultation

11.1 Consultation will occur with country partners to ensure the design of the window is appropriate and feasible. This will be coordinated through a dedicated JE sub-team set through the Vaccine Implementation team.

11.2 Suppliers will also be consulted in the development of a roadmap for JE vaccines.

12 Gender implications

12.1 Boys and girls will be equally targeted for JE campaigns.

Section D: Annexes

Annex A: Annex to the September 2011 PPC paper on Japanese Encephalitis Implementation Strategy.

Implementation Strategies and New Windows — Japanese Encephalitis

- 1.1 JE is a public health concern in Asia. The disease has a high fatality rate (up to 30%), and 20-40% of cases develop long-term neurological sequelae.⁷ There is no specific medical treatment, and vaccination is the single most important control measure.
- 1.2 While reported cases of JE to WHO remain low (8,287 in 2010), estimates range between 50,000 - 100,000 cases of clinical JE. A recent analysis based on publications of laboratory-confirmed cases estimates that approximately 66,300 cases occur each year.
- 1.3 There is no medical treatment for JE infection. Vector control efforts have had limited success in controlling JE, primarily due to the need for continuous control measures. As a result, prevention of clinical JE through vaccination is the best strategy to control JE.

Disease Burden — JE

Japanese encephalities , countries or areas at risk, 2008



Figure 1

Source: World Health Organization Map Production: Public Health Information and Geographic Information Systems

⁷ WHO Press Bulletin, November 2011

2. WHO position paper and SAGE recommendations

- 2.1 The current WHO position paper recommends that the most effective immunisation strategy in Japanese encephalitis (JE) endemic settings is a one-time catch-up campaign in children between the ages of 9 months and 15 years in at-risk populations, followed by incorporation of JE vaccines into routine childhood immunisation. There are no documented herd effects with JE vaccination.

Global Recommendations for JE vaccines

- 1) **One-time catch-up campaign in under 15 year olds in at-risk populations**
- 2) **Incorporation of JE vaccines into routine childhood immunisation programmes**

3. GAVI support for JE vaccine introduction

- 3.1 GAVI will pay for a one-time catch-up campaign in 9 month to 15 year olds.⁸ The support will be for the vaccine cost, syringe and safety box, and shipment costs. The catch-up quantities are based on the targeted number of children in the 14 birth cohorts between 9 months of age to 15 years of age. The catch-up would be carried out over 12 months, which can take place over more than one calendar year.
- 3.2 In addition, GAVI will also pay for introduction grants for each country to encourage the integration of JE into national immunisation programmes in the 9 month - 1 year old cohort starting after catch-up completion.
4. **Target countries** — Eight countries from South and Southeast Asia with high-burden of disease.

Target Countries

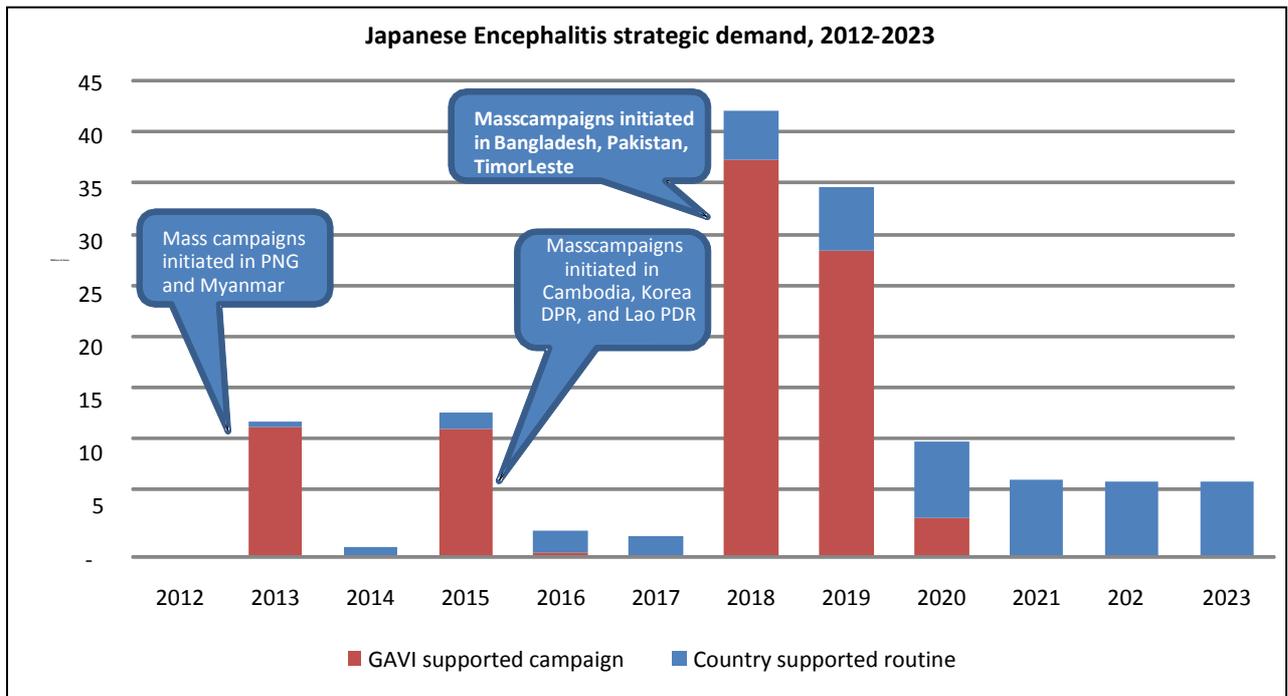
Eight countries: Bangladesh, Cambodia, Democratic People's Republic of Korea, Laos, Myanmar, Papua New Guinea, Pakistan, Timor-Leste.

⁸ Countries are free to apply for up to 100% of the birth cohort, although this may be less in countries where coverage is anticipated to be lower.

5. Target population

The target population for the campaign includes children from 9 months to 15 years of age. JE can affect anyone at any age but the majority of cases have been reported in children up to 15 years of age.

6. Demand — JE



No. of introductions by year	2012	2013	2014	2015	2016	2017	2018	2019	2020	Total
JE	0	3	0	2	0	0	3	0	0	8

7. Market Analysis — Japanese Encephalitis

7.1 Supply landscape: Mouse brain-derived JE vaccines were developed in the 1950s but had safety issues due to the process and materials used and were priced at approximately US\$ 4.50 per dose for a three dose course⁹. There is currently no WHO pre-qualified JE vaccine. For low income countries, the current momentum is for the development of live attenuated vaccines, especially on Chengdu’s SA 14-14-2 vaccine supported through PATH, for which WHO pre-qualification is expected in 2013. For Chengdu’s SA-14-14-2, one dose needs to be given to over 9 month old children and its shelf life is currently 18 months, with

⁹ Prices are quoted as ex-manufacturer or “unloaded” costs, excluding freight, syringes, safety boxes, and further downstream costs

work under way to extend it to 24 and 36 months planned for completion in 2015. Other vaccines based on different technologies (inactivated or chimeric) are also licensed or under development by a wide variety of manufacturers. These products are for over 12 month old children (although some are conducting trials for younger age groups) and have or expect to have a dosage of 1 or 2 doses per course. WHO pre-qualification could be achieved for inactivated vaccines in 2013-2014. The chimeric vaccine is targeting WHO pre-qualification in 2012.

7.2 Impact on the supply landscape of the recommended GAVI support:

The profile of country demand for JE vaccines would be met through the planned supply capacity from Chengdu. Chengdu is receiving significant support from PATH to ensure sufficient capacity to meet global demand and to achieve WHO pre-qualification, which is currently under way and expected to conclude in 2013. A new GMP facility dedicated to JE vaccine production has been built and there is potential to further expand capacity with additional investment in fill-finish lines and freeze-drying capacity. However, a potential risk remains that in the event of a supply constraint situation, priority may be given to the domestic market over the export GAVI market. Live-attenuated vaccine from Chengdu has been sold at less than US\$ 0.40 per dose (one dose course). This price range has allowed some Low Income Countries and Lower Middle Income Countries to introduce JE vaccination already without financial assistance. The collaboration with PATH has set price ceiling for SA 14-14-2 for the Low Income Country LIC public sector, with established guidelines for price increases. Other JE vaccines, inactivated and chimeric, are characterised by higher (>US\$ 1) and widely varying price points depending on the technology used and manufacturer.

7.3 Implications for GAVI supply and procurement: There is currently no vaccine with WHO pre-qualification, and there are no vaccines for purchase under US\$ 1.00 per course for GAVI countries until the SA 14-14-2 becomes WHO pre-qualified. Therefore, the preferred GAVI option is for Chengdu's product. GAVI recognises that the manufacturer is as yet an unproven supplier to GAVI countries and will mitigate the risks of sole source procurement, such as production or quality risks, through its supply and procurement strategy.

8. Surveillance and Post-Introduction Monitoring

- 8.1 JE surveillance is critical to characterize epidemiology, measure burden of disease, identify high-risk areas as well as document the impact of control measures.
 - 8.2 Impact and local data will help to better define sub-sets of the population for vaccination programmes. Countries should consider implementing JE surveillance in conjunction with invasive bacterial disease (IBD) and rotavirus surveillance to leverage resources and programmatic goals.
 - 8.3 Improved monitoring of AEFI should also be put in place.
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