

## Meningitis Investment Case

### Background

At the November 2007 meeting, the GAVI Alliance and Fund Boards reaffirmed the prior board decision to prioritise meningitis A vaccine and agreed that it should be considered outside of the vaccine investment strategy process. The Board requested the GAVI Secretariat to initiate the submission and independent review of a meningitis investment case resulting in recommendations to the Board at their June 2008 meeting. The investment case addresses the GAVI strategic goals of strengthening the capacity of the health system to deliver immunisation and other health services in a sustainable manner and accelerating the uptake and use of new vaccines and associated technologies and improving vaccine supply security.

The GAVI Alliance Secretariat established an Independent Review Committee (IRC) to carry out an independent review of the meningitis investment case. The members of the IRC had strong developing country representation and high level expertise in the areas of epidemiology, vaccine and child health research, immunization services, health systems, applied economics and health financing. The investment case was also reviewed by the GAVI Working Group and the GAVI Secretariat whose comments were shared with the IRC.

### Objective

Meningitis epidemics affect a limited number of countries located in the African Meningitis Belt (See Annex 1 for map of countries). During 1996 and 1997, serogroup A meningococcal (Nm A) epidemics caused more than 250,000 meningitis cases, 25,000 deaths, and residual disabilities among 50,000 persons. From 1997 to 2007, 653,400 cases and 59,600 deaths due to meningitis were reported. Approximately 90 percent of meningitis epidemics are due to serogroup A *Neisseria meningitidis*.

The Meningitis Vaccine Project (MVP), a partnership between WHO and PATH with core funding from the Bill & Melinda Gates Foundation, was formed in 2001 to develop, test and license meningococcal conjugate vaccines for sub-Saharan Africa. Out of these efforts, an affordable Meningococcal A (Men A) conjugate vaccine manufactured by Serum Institute of India, Ltd. was developed. At less than US\$0.50 per dose, the vaccine is immunogenic in both adults and infants and expected to confer long-term protection. Licensure and WHO prequalification are expected by the end of 2009 for persons one year or older; an infant indication is expected by 2012.

Currently available meningococcal polysaccharide vaccines have three significant limitations that make them poor candidates for preventive vaccine strategies: they do not protect children under one year of age, the immune protection they provide lasts only up to three years, and they do not protect unvaccinated people by impacting bacterial transmission. However, during the roll-out phase of Men A conjugate vaccine introduction, Nm A epidemics could still occur in countries that have not yet received the conjugate vaccine so a sufficiently large and accessible stockpile of Men Ps vaccines for epidemic response is proposed to ensure protection of at-risk populations and improve epidemic response.

The objectives of the proposed investment case are to:

- Eliminate Meningococcal A meningitis epidemics in the most affected 25 African countries<sup>1</sup> home to an estimated 95 percent of the world's meningococcal meningitis disease burden
- Facilitate introduction of a Meningitis A conjugate vaccine through preventive mass vaccination campaigns and routine immunization strategies
- Provide long-term direct protection to approximately 272 million people
- Prevent approximately 149,000 deaths by 2015
- Prevent permanent disability in approximately 347,000 children and adults and alleviate the related social and economic burden
- Prevent 13 million DALYs lost
- Save approximately \$121 million in medical costs for diagnosis and treatment

### Investment case activities

The investment case focuses on an integrated program that seeks to rapidly eliminate epidemic serogroup A meningococcal (Nm A) meningitis as a public health problem in sub-Saharan Africa. The proposed activities will also reduce non-epidemic Nm A meningitis and improve the effectiveness of public health response to meningitis epidemics.

The governments of countries in the African Meningitis Belt, public health experts from WHO, UNICEF, the World Bank, the Bill & Melinda Gates Foundation, and the Meningitis Vaccine Project (MVP)—and regional and national institutions are committed to meeting this objective. A four-component plan for ending recurring Nm A meningitis epidemics in Africa and improving epidemic response was developed in partnership with these groups:

**Preventive conjugate vaccine introduction.** This component involves introducing a meningococcal A conjugate (Men A conjugate) vaccine to immunize a population of approximately 250 million 1- to 29-year-olds and 23 million infants living in up to 25 GAVI-eligible African countries from 2009 to 2015. The effort will protect up to 400 million people through herd immunity that is likely to follow introduction of the Men A conjugate vaccine. Activities include:

- An initial mass vaccination campaign in the 1-29 year-old population with a target coverage of 90 percent to establish population immunity in high-risk age groups.
- Vaccination of birth cohorts following the initial mass campaigns through routine EPI and follow up campaigns

The 1-29 year old target population which makes up about 70% of the total population was chosen because it suffers the highest attack rate from invasive meningococcal disease. In addition, this age group has traditionally been identified as the “target group” for reactive vaccinations with polysaccharide vaccine, as well as for preventive vaccinations undertaken in some countries. African populations are thus accustomed to mass vaccinations in this age group and have been able to achieve high coverage in this age group. A mass campaign in 1 to 29 year olds with a Men A containing conjugate vaccine in sub-Saharan Africa would be expected to accomplish three goals:

- Eliminate epidemic meningitis due to group A *N. meningitidis*
- Reduce the rate of endemic meningitis by 50 percent (the fraction of endemic meningitis due to group A *N meningitides*)

<sup>1</sup> Benin, Burkina Faso, Burundi, Cameroon, Central African Republic, Chad, Côte d'Ivoire, Democratic Republic of the Congo, Eritrea, Ethiopia, The Gambia, Ghana, Guinea, Guinea Bissau, Kenya, Mali, Mauritania, Niger, Nigeria, Rwanda, Senegal, Sudan, Tanzania, Togo, Uganda

- Establish herd immunity with control of group A *N. meningitidis* in infants and persons above 30 years of age

Although there is some perceived risk to routine services with the implementation of a mass campaign, this risk has been appropriately handled in cases such as measles. Further, at present, countries are currently faced with mounting emergency meningitis polysaccharide vaccine campaigns, while at the same time managing the increased cases of severe hospitalized epidemic meningitis. Thus, the ability to plan for a truly preventive campaign, which is planned to be conducted in a matter of days, may in fact reduce the extent of disruption on routine health service resources. In addition, as shown for measles vaccination campaigns, it is likely that preventive meningitis mass vaccination - by reaching otherwise unreached populations - will increase communities' awareness of immunization services and actually increase routine coverage.

**Epidemic response.** This component centers on ensuring that adequate quantities of meningococcal polysaccharide (Men Ps) vaccines are available by establishing epidemic response stockpiles and improving timeliness of response. The main activity is to secure and maintain appropriate vaccine stockpiles.

**Case-based surveillance, risk assessment, and Men A conjugate vaccine impact assessment.** Specific activities in this component are to strengthen the current enhanced surveillance system of meningitis, establish case-based surveillance, guide the introduction of Men A conjugate vaccine through risk assessment, monitor meningitis epidemiology, and document the impact of this vaccine on epidemic Nm A meningitis.

**Country-level capacity-building.** Activities in this component will ensure that adequate national and regional capacity exist for the implementation of the plan, including preventive conjugate vaccine introduction, epidemic response, and case-based surveillance and risk and impact assessment.

## Financial implications

It is important to note that GAVI is not being asked to fund the full cost of the activities; the investment case developers have determined that GAVI funding should be catalytic. For example other organizations which have been identified to provide funding include:

- National governments: half of mass campaign delivery costs; all routine immunization delivery costs, infrastructure, and systems; co-pays for bundled vaccine purchase for EPI immunization
- Local communities and regional/local health systems: economic/opportunity costs
- The Bill & Melinda Gates Foundation, through MVP: enhanced surveillance through 2010 and design/planning for the first introduction in Burkina Faso
- The Michael and Susan Dell Foundation: support to Burkina Faso for purchasing vaccines and injection supplies, strengthening national vaccine delivery and surveillance systems, and documenting public health impact and operational lessons learned to support roll-out to other countries
- EuropAid Cooperation Office (AIDCO): support to countries and implementation of AEFI surveillance in west and central Africa from 2009-2010
- Foundation, bilateral organization, and development banks (including USAID, the African Development Bank, and the Islamic Development Bank) are expected to contribute to operational costs of national mass campaigns through country funding baskets

- Other funding sources to be identified in relation to linked studies and impact assessment activities

The following three tables summarise the total cost of the project, requested financing over the proposed investment period of 2009-2015, and provide breakdowns by proposed recipients and by year.

**Table 1: Project costs and amount requested from GAVI**

Component	Total cost	Request from GAVI
Preventive conjugate vaccine introduction:		
• Conduct mass campaigns to vaccinate up to 236 million 1-29 year olds	\$377.2 million	<b>\$245.6 million</b>
• Introduce Men A conjugate vaccine into EPI programs (estimated 23 million infants)	\$45.2 million	<b>\$23.4 million</b>
• Implement follow-up campaigns with Men A conjugate vaccine	\$21.3 million	<b>\$11 million</b>
Vaccine stockpile and reactive campaigns	\$86.3 million	<b>\$55.2 million</b>
Conduct case-based surveillance, risk assessment, and Men A conjugate vaccine impact assessment	\$14.9 million	<b>\$12.2 million*</b>
Provide country-level capacity-building	\$26 million	<b>\$23 million*</b>
<b>TOTAL</b>	<b>\$571 million</b>	<b>\$370 million</b>

\* These amounts may include overlap with other pending requests to GAVI, in particular the accelerated vaccine introduction initiative (AVI) and the work plan.

**Table 2: Proposed recipients of GAVI funds**

Proposed recipient	Budget
<b>Ministries of Health:</b> Vaccine introduction for countries introducing Men A conjugate vaccine into their EPI programme	\$1.2 million
<b>UNICEF Supply Division:</b> to purchase and shipment of vaccines to approved countries	\$231 million
<b>WHO:</b> for pass-through to countries for operations of campaigns, technical assistance and operations in support of mass campaigns, reactive campaigns, surveillance, impact assessment	\$137 million*
<b>TOTAL</b>	<b>\$370 million</b>

\* These amounts may include overlap with other pending requests to GAVI, in particular the accelerated vaccine introduction initiative (AVI) and the work plan.

**Table 3: GAVI Financing by Year (US \$'000)**

2009	2010	2011	2012	2013	2014	2015	TOTAL
27,531	32,717	57,911	58,346	67,412	62,477	63,843	370,236

The investment case also notes that there are potential areas of overlap between the investment case activities and proposed Accelerated Vaccine Introduction (AVI) and work plan activities. In light of this, the IRC recommended that a further review of the budget be done to assess the assumptions and justifications for costs as well as clarification around potential overlaps with other funding streams.

## Monitoring, evaluation & risks

The definition of success for this project is the cessation of Nm A epidemics in the African Meningitis Belt countries that have introduced the Men A conjugate vaccines. This project will be evaluated using the following indicators:

**Process indicators:**

- Availability rate of vaccines at country level (target: 100 percent).
- Wastage rates during mass campaigns and routine activities (target: <15 percent).
- Vaccination coverage in the target population achieved during the national mass campaign in elected countries (target: >90 percent of 1- to 29-year-olds).
- Vaccination coverage in the target population achieved during the follow-up campaign in elected countries (target: >90 percent of 1- to 5-year-olds).
- Vaccination coverage in the target population for routine immunization (target: >90 percent of 0- to 1-year-olds).
- Proportion of countries implementing plans for AEFI surveillance of Men A conjugate vaccine (target: 90 percent)
- Proportion of countries implementing their surveillance plan (target: 90 percent).
- Proportion of districts fully implementing plans for disposal of wastes within two weeks of mass campaign (target: 80 percent).
- Proportion of districts conducting reactive mass campaigns within two weeks of reaching the alert or epidemic thresholds (target: < 2 weeks).
- Availability rate of vaccines at country and district levels (target: 100 percent at all levels).
- Wastage rates (target: < 15 percent).
- Vaccine coverage in the target population achieved during reactive mass campaigns (target: >90 percent for 2- to 29-year-olds).
- Proportion of districts conducting reactive mass campaigns within two weeks of reaching the alert or the epidemic thresholds (target: 90 percent).
- Proportion of districts fully implementing plans for disposal of waste within two weeks of mass campaign (target: 80 percent).
- Proportion of countries implementing plans for AEFI surveillance of Men A conjugate vaccine (target: 90 percent)
- Proportion of countries producing weekly case reports for suspected bacterial meningitis (target: 100 percent).
- Epidemiologic reports on meningitis cases indicating laboratory confirmation (target: 90 percent).
- Proportion of epidemic health districts for which laboratory investigation was conducted (target: 100 percent).
- Proportion of countries with two geographically distinct sentinel sites where individual clinical and laboratory data are available (target: 80 percent).

**Outcome indicators:**

- Number of districts reporting meningitis cases due to Nm A.
- Frequency of Nm A among isolated infectious agents.
- Number of deaths associated with Nm A during epidemics.

**Table 4: Risks**

Risk	Risk minimization
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Inadequate country funding and support for Men A conjugate vaccine introduction in a hyperendemic country (undermining protection across all hyperendemic countries)	<ul style="list-style-type: none"> <li>• GAVI support to motivate countries and other donors</li> <li>• Close collaboration on meningococcal conjugate vaccine development since 2001</li> <li>• Advocacy and information to support country planning and decision-making</li> <li>• Regional technical assistance</li> </ul>
Weak delivery systems in a hyperendemic country means low coverage (<70%) of mass campaigns and precludes herd immunity	<ul style="list-style-type: none"> <li>• Regional technical assistance</li> <li>• Strong advocacy and communication</li> </ul>
Large meningitis epidemic in 2008–2009	<ul style="list-style-type: none"> <li>• Enhanced surveillance and alert systems and epidemic response vaccine stockpile can mitigate damage and spread of epidemic.</li> <li>• A crisis plan for this situation will help guide decision making.</li> </ul>
Rumors about vaccine impact or safety.	<ul style="list-style-type: none"> <li>• A national communication strategy, including journalist workshops, will be established prior to introduction</li> <li>• Comprehensive data and information will be presented to MOHs, community leaders, and others</li> </ul>

## IRC Recommendations

The IRC strongly recommended that the Meningitis Investment Case be supported by GAVI, and strongly endorsed the strategic components of the case (see Annex 2 for IRC report). The IRC also recommended that the Board have a specific review of the budget to assess the assumptions and justifications for costs and endorsed GAVI efforts to implement the case effectively and efficiently. The IRC requested stronger budget justification and clarification around potential overlap areas with HSS, ISS and other systems and noted that the budget for capacity building had little specificity for what the actual investment would be.

Members of the IRC found the investment case to be sufficiently clear, accurate and credible and supported GAVI principles in the following way: The proposed efforts are around a new vaccine that is a country-defined priority. The elimination of group A Meningococcal epidemics in the proposed target area would make a significant contribution to the attainment of MDGs 1, 4 and 5. The main components of the investment case would be time-limited efforts. Efforts have been made to make the vaccine affordable to countries to encourage future financial sustainability.

The IRC also found that there is a high probability that the proposed investment can successfully achieve at least 75% of the stated project objectives. In this regard, the IRC strongly noted several points during their review:

- **Preventive campaign strategy:** The proposed conjugate vaccine campaign strategy has strong potential for eliminating circulating nasopharyngeal carriage of Meningococcal group A strains and would be an excellent investment for preventing epidemics in concert with introduction of the conjugate vaccine into the EPI as long as there is continued high EPI coverage. The considerable experience of conducting mass campaigns for polio and measles and the high political support in the region offer high potential for success.
- **Follow up campaign strategy:** The proposed strategy of follow up campaigns would provide an appropriate mechanism to immunize children excluded during the catch up campaign because of being under one year and those missed by routine immunization

coverage. However, this should be a time-limited strategy. Once there is infant licensure, maintaining infant coverage through routine EPI should be the strategy of choice.

- **Stockpile:** The IRC noted the importance of the stockpile to ensure a steady supply of vaccine and speediness of responses to epidemics and accepted the appropriateness of the approach defined in the investment case. Specifically the IRC supported the approach of keeping the polysaccharide vaccine in the stockpile for epidemic responses, but noted that this strategy might change over time should sufficient quantities of the conjugate vaccine becomes available.
- **Interagency group (ICG) composition:** The IRC understands the efficiency of having a single body (ICG) make decisions on 1) sequence of countries to implement preventive campaigns (after the first three high risk counties) as well as 2) use of stockpile for emergency response. The IRC strongly endorsed that the supplementary members added to the ICG to provide “technical support” also have decision making authority with the rest of the ICG on all ICG decisions involving conjugate vaccine. The IRC also noted the importance of ICG having input from GAVI and appropriate partners.
- **Country involvement:** Country consultation should continue as noted in the investment case. The IRC noted the importance of clarifying the implementation strategy and approach for decisions on country introduction.
- **Case based surveillance:** The IRC noted that strengthening of disease surveillance has been undertaken through MVP and efforts to improve need to be continued. The IRC noted that this is dependent on fundamental systems strengthening and a concerted effort at country level including training health care workers to get appropriate diagnostic testing and report cases, as well as increasing laboratory based diagnosis. Because the conjugate vaccine is new, the IRC encouraged of implementation of a Phase IV trial to formally obtain effectiveness data. The IRCs strongly endorsed the investment by GAVI for surveillance of the disease..
- **Adverse effects following Immunization (AEFI):** The IRC strongly endorsed the importance of ongoing monitoring of AEFI and supported the suggestion of special studies, including possible Phase IV studies on the new vaccine roll out. The IRC also endorsed strengthening the capacities of National Regulatory Authorities to allow them to evaluate vaccines for licensure and to conduct post-introductory surveillance. The IRC strongly endorsed WHO ongoing activities in this regard.
- **Timelines for licensing and prequalification:** The timeline for obtaining licensure and prequalification of the vaccine in the same year as well as for the implementation of the programme is ambitious and the timeline for the entire investment case rests on prequalification. The IRC endorsed the concomitant encouragement of partners to accelerate the WHO prequalification process.

### Context of Meningitis investment case consideration

In recent years GAVI has made decisions about its new programmatic investments based on an investment case framework. In order to make best use of the available resources – and to ensure maximum impact, the Boards recognised the need for a comprehensive vaccine investment strategy that would define which new vaccines GAVI will consider supporting over the next five years. Based on a comprehensive analysis and a broad consultation including review by the Independent Review Committee for the GAVI Alliance vaccine investment strategy, Meningitis A vaccine is being recommended for inclusion in GAVI’s vaccine portfolio at this Board meeting.

It should be noted that the value of the meningitis investment case has not been thoroughly compared relative to other past and future GAVI investments. Although some initial analysis on opportunity costs has been undertaken as part of the vaccine investment strategy, the full case on a range of investment options will not be presented to the board until October. The lack of this

information at this time makes it difficult to make thorough comparisons regarding cost effectiveness.

The table below shows comparative cost effectiveness between various vaccination strategies as outlined in their respective investment cases. It also shows initial disease mortality data compiled for the GAVI Vaccine Investment Strategy for diseases for which GAVI has funded investment cases. What it does not capture is the epidemic potential of meningitis that in 1996 and 1997 alone resulted in 25,000 deaths.

**Table 5 Comparison of impact of meningitis A investment case to other GAVI-supported vaccine investment cases\***

	Cost per DALY averted	Cost per death averted	Annual mortality in GAVI eligible countries**
Meningitis	\$37	\$2,218	3,000
Pneumococcal	\$22	\$691	905,000
Rotavirus	\$15	\$600	495,000
Measles	\$15	\$499	n/a
Yellow Fever	\$12	\$437	1,000

\*Assumptions vary tremendously among investment cases and the data may have changed since they were initially presented.

\*\* Compiled for GAVI Vaccine Investment Strategy. April 2008

## Board request

The GAVI Alliance and Fund Boards are requested to:

- Approve the strategy outlined in the Meningitis investment case.
- Delegate authority to the Secretariat to conduct an in-depth review of the budget, up to an envelope of \$370.8 million, and define the specific amounts in funding agreements with WHO and UNICEF to implement their components of the strategy.

or

- Determine that a final decision to fund this programme be taken alongside other vaccines at the October 2008 Board meeting.

# ANNEX 1

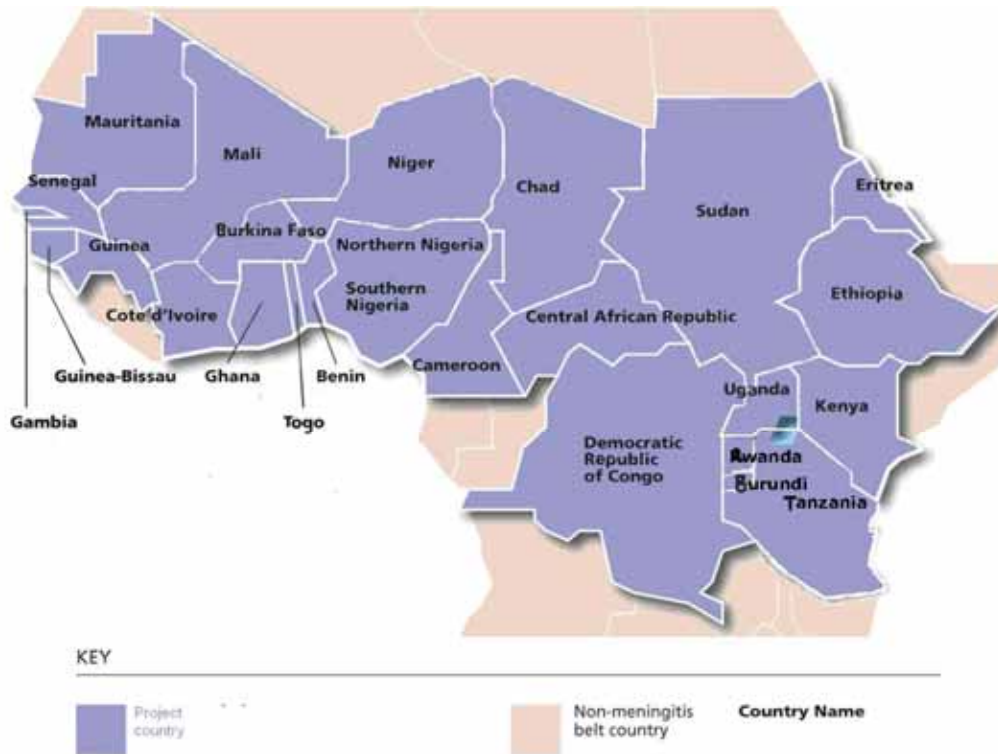


Figure 1. The African Meningitis Belt and project countries.

**ANNEX 2**

**Independent Review Committee  
Yellow Fever Continuation and Meningitis investment cases  
Amsterdam, Netherlands  
27 – 28 May 2008**

**Meeting Report for Review of Meningitis Investment Case**

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### **INDEPENDENT REVIEW COMMITTEE**

The Independent Review Committee (IRC) met over the course of two days in Amsterdam to review the yellow fever continuation and meningitis investment cases and make recommendations to the Board. The IRC commended the investment case preparers for their extensive work on the investment cases. The Chair of the IRC also commended the IRC members for their thoughtful and thorough discussion. The IRC consisted of the following members:

- Dr. Claire Broome (Chair), Epidemiologist and Public Health Specialist, USA
- Dr. George Amofah, DG and Director of Public Health of Ghana Health Service, RBM
- Professor Diana Lennon, Professor of Population Child & Youth Health, The University of Auckland, New Zealand
- Dr. Grace Murindwa, Health Planner and Management Specialist, Uganda
- Dr. Ahmed Bedru Omer, Clinical Trial Coordinator, Armauer Hanseon Research Institute, Ethiopia
- Professor Helen Rees, Executive Director, Reproductive Research Unit, University of Witwatersrand, South Africa

The Terms of Reference (TORs) for the IRC mandated members to review the investment cases with the following overall objectives:

- Provide the GAVI Alliance and Fund Boards with information so it can determine whether a given investment fits with overall GAVI Alliance and Fund principles
- Ensure that basic data analyses are available to the Board for evidence-based decisions on the use of limited GAVI Fund resources.

### **MENINGITIS INVESTMENT CASE DISCUSSION**

The IRC had an initial review and discussion of the meningitis investment case. After this review, a teleconference was conducted with the investment case authors. Following the teleconference, discussion continued. Overall, the IRC commended the investment case preparers for their excellent work and the strong presentation of the strategic components of the case. Through the discussions and the teleconference, the following points were raised.

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**Preventive campaign for 1-29 year olds:** There was strong consensus on the importance of the preventive conjugate vaccine campaign strategy for its expected impact on mortality and in preventing devastating epidemics in meningitis belt. The Committee acknowledged that traditional campaigns have not necessarily been a preferred GAVI strategy, but it was noted that the proposed campaign strategy in the investment case had strong potential for eliminating circulating nasopharyngeal carriage of Meningococcal group A strains and felt that the intervention would be much more effective if campaigns were conducted in a broad manner up front and continued with high EPI coverage.<sup>2</sup>

**Follow up campaigns for 1-4 year olds:** The IRC noted follow up campaigns would provide an appropriate mechanism for those children that would be missed by routine immunization as the vaccine would not be available for infant indication for another several years. The IRC felt this way especially to improve community understanding of the vaccine. There was discussion on the cost effectiveness of the follow up campaigns, but it was agreed that the strategy was still important, especially in light of the relatively low cost scale for these campaigns. The IRC noted that these follow up campaigns should be a time-limited strategy and that routine EPI is critical and important in maintaining herd immunity. The IRC noted that once there is infant licensure, maintaining infant coverage through routine EPI should be the strategy of choice.

**Polysaccharide vaccine and stockpile:** The IRC noted the importance of the stockpile because of the high likelihood of epidemics in the interval before the 1-29 preventive campaigns are implemented and the availability of a stockpile is one method to ensure availability of vaccines and speed of responses to epidemics. The IRC acknowledged the risk of depending solely on conjugate vaccine for the stockpile because of certain unknowns regarding supply and demand, thus the need to assure a supply of polysaccharide vaccine as an interim measure; the multi-valent polysaccharide vaccines also provide coverage for group C or W-135 outbreaks if those should recur, and provides market stability for availability of the polysaccharide vaccine. The IRC noted that this was an appropriate approach, but also noted that the stockpile was larger than the doses distributed by the ICG in recent years – although that number may have been artificially low due to vaccine shortage. The investment case authors clarified with the IRC that after 2013, the stockpile would not be needed at the same levels as in earlier years because the number of epidemics at that point will be minimal.

**Interagency Coordinating Group (ICG) composition and process:** It is proposed in the investment case that the ICG will make decisions regarding country proposals for preventive campaigns as well as emergency responses. It was clarified on the teleconference that it is intended that supplementary members added to the ICG for “technical support” will have decision making powers. The IRC strongly endorsed technical experts having decision making authority and recommended that they be involved with all aspects involving conjugate vaccine (including if/when used for emergency response). The IRC also noted the importance of ICG having input from GAVI and appropriate partners. In addition, the IRC noted the importance of balanced consideration of preventive strategy and emergency response and noted that processes for emergency response should be designed to accelerate, not slow down use of stockpile.

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<sup>2</sup> It was noted that Annex C was not expanded as explained in the investment case

## ANNEX 2

**Decisions regarding country introduction of vaccine:** The IRC noted the importance of clarifying the implementation strategy and approach for decisions on country introduction. The IRC agreed with the approach for the first three countries. It was clarified on the teleconference that following the first three countries, introduction will be done on a country basis (not by percentage of population of all countries as statement was ambiguous in the investment case). Decisions on EPI introduction into an entire country or just at-risk areas will be dependent on country-level consultation. The IRC strongly endorsed consulting countries on the approach to be taken and noted that the extent of country consultation in preparing the investment case was a strength of this proposal.

**Case based surveillance:** There was discussion regarding the importance of both clinical case based and laboratory confirmed case surveillance. The IRC noted that strengthening of disease surveillance has been undertaken through MVP and efforts to improve need to be continued. The IRC noted that this is dependent on fundamental systems strengthening and a concerted effort at country level including training health care workers to get appropriate diagnostic testing and report cases. The IRC also noted the importance of preserving the funding in the investment case for surveillance of the disease.

**Adverse effects following Immunization (AEFI):** The IRC emphasized the importance of monitoring AEFI given that this vaccine is a new product for this manufacturer. The IRC clarified with the investment case authors that special studies and monitoring of AEFI is occurring during the MVP studies. The IRC noted the importance of tracking rare side effects by sensitizing health providers in area and the provision of forms and procedures for reporting AE. The IRC also thought that it would be important to strengthen authorities' ability to conduct post surveillance and maintain strong linkages with WHO on regulatory strengthening.

**Budget:** The IRC recommended that the Board have an additional review of the budget to assess the assumptions and justifications for costs and endorsed GAVI efforts to implement the case effectively and efficiently. The IRC especially felt a need for stronger budget justification around potential areas for overlap around HSS, ISS and other systems. They noted that the budget for capacity building had little specificity for what the actual investment would be.

**Timelines for licensing and prequalification:** Some concern was expressed on the ambitious timeline for obtaining licensure and prequalification of the vaccine and implementation of the programme especially since the initiation of the investment case rests on the assumed timeline. The IRC recommended, as possible, the concomitant encouragement of partners to accelerate the WHO prequalification process, including support of Indian NRA.

**Implementation with other initiatives:** The IRC also recommended that, as feasible, countries consider implementing these strategies with other initiatives (e.g. measles campaigns).

### RECOMMENDATIONS TO THE BOARD

The IRC strongly recommended that the strategic components as described in the Meningitis Investment Case be supported by Board and also recommended that the Board have a specific

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review of the budget to assess the assumptions and justifications for costs and endorsed GAVI efforts to implement the case effectively and efficiently. The IRC felt a need for stronger budget justification around potential overlap areas with HSS, ISS and other systems and noted that the budget for capacity building had little specificity for what the actual investment would be.

Members of the IRC found the investment case to be sufficiently clear, accurate and credible. The IRC found the investment case to be consistent with GAVI principles: The proposed efforts are around a new vaccine that is a country-defined priority. The elimination of group A Meningococcal epidemics in the proposed target area would have a significant impact on MDGs. The main component of the investment case, the preventive campaigns, would be a one-time investment. Efforts have been made to make the vaccine affordable to countries to encourage future financial sustainability for use in routine EPI. Finally this investment is actually cost-saving because it will eliminate the need for a stockpile and epidemic response activities which are costly to both the countries' health infrastructure and the global donor community.

The IRC also found that there is a high probability that the proposed investment can successfully achieve at least 75% of the stated project objectives, although the objective for emergency vaccinations within two weeks of crossing the epidemic threshold is exceedingly ambitious.