



Report to the GAVI Alliance Board

11-12 June 2013

Subject:	Vaccine Investment Strategy
Report of:	Nina Schwalbe, Managing Director, Policy and Performance
Authored by:	Judith Kallenberg, Senior Specialist, Vaccine Investment Strategy and Aurelia Nguyen, Director, Policy and Market Shaping
Agenda item:	06
Category:	For Decision
Strategic goal:	Affects all strategic goals

Section A Overview

1 Purpose of the report

- 1.1 This report seeks Board approval of the recommendation by the Programme and Policy Committee to narrow the list of vaccines under consideration for the Vaccine Investment Strategy (VIS) on the basis of criteria for health impact, epidemic potential and value for money. The paper discussed by the PPC, which includes details on the recommendations, the strategy development process, vaccine evaluation criteria and prioritisation approach, is attached to this note.
- 1.2 Following Board decision, the Secretariat will proceed with further analysis of shortlisted vaccines and, in consultation with the Technical Consultation Group and Independent Expert Committee, request a PPC recommendation in September for future vaccine priorities (additional to the current GAVI portfolio) for Board decision in November.

2 Executive Summary – Update since the April 2013 PPC meeting

- 2.1 The Secretariat, with input from expert consultations, generated preliminary impact and cost estimates to facilitate a comparison between vaccines in the list provided by the World Health Organization (WHO).
- 2.2 The PPC recommends that vaccines with a relatively high potential for health impact (including impact on mortality and on the risk of epidemics) and relatively low cost per death averted are further analysed in phase II of the strategy development process. These include malaria, influenza (for maternal immunisation), rabies, cholera and yellow fever vaccines (mass campaigns), as per option 2 in the PPC paper. This recommendation, which deprioritises vaccination strategies with lower health impact and/or

higher cost for impact achieved (dengue, hepatitis A, hepatitis B birth dose, hepatitis E, measles for an expanded age cohort, and meningitis serogroups CYW), is consistent with feedback from an Independent Expert Committee as reflected in annex B of the PPC paper. The decision to prioritise vaccines for further evaluation in phase II does not constitute an investment decision.

- 2.3 Demand and cost estimates (for shortlisted vaccines) will be updated in phase II to take into account 1) other/existing vaccine introduction priorities, 2) refined implementation scenarios, 3) operational feasibility, 4) country preferences, and 5) supply constraints.
- 2.4 Impact estimates will be updated based on new data and improved modelling approaches where available.
- 2.5 Final recommendations in November will be based on a comparison with existing GAVI vaccines. The PPC supported the proposed approach for phase II and additionally requested that the degree of uncertainty around future vaccine availability and product characteristics is reflected in the recommendations.
- 2.6 An investment in inactivated polio vaccine (IPV) does not compare favourably to other vaccines based on direct measures of health impact (e.g. deaths averted). However, IPV has unique value as a critical component of the global polio eradication effort. The PPC therefore considered an investment in IPV outside the evaluation framework developed for other vaccine candidates in the VIS. The PPC recommended that preparations are initiated for investment in IPV in anticipation of a definitive funding commitment. This decision is the subject of Doc 07.

3 Recommendations

- 3.1 The Programme and Policy Committee recommends to the Board that it:
 - (a) **Endorse** the evaluation criteria set out in Table 1 in Doc 07 for consideration in the Vaccine Investment Strategy (VIS) process;

- (b) **Decide** to narrow the choice of possible vaccine investment options (in addition to GAVI's current portfolio) for further analysis in Phase II by prioritising vaccines based on health impact (mortality and morbidity), epidemic potential, and value for money (procurement cost per death averted). The Phase II analysis outcomes shall be benchmarked against the vaccines in GAVI's current portfolio. As modelled in Phase I of the VIS and subject to further analysis in Phase II, influenza (for maternal immunisation), malaria and rabies vaccines are in the top tier of health impact outcomes; cholera and yellow fever vaccines are included on the basis of epidemic potential and value for money outcomes. Dengue, meningitis (serogroups CYW135) and measles (expanded investment), while diseases with epidemic potential, are excluded from further analysis because of a relatively high cost per death averted of the modelled strategy;
- (c) **Request** the Secretariat – recognising the urgency of timing in the polio eradication effort and that considerations for Inactivated Polio Vaccine (IPV) are not consistent with the VIS criteria or timing – to prepare for procurement and implementation of GAVI support for the introduction of IPV in the routine immunisation programmes of GAVI countries as recommended by WHO as a contribution to polio eradication. These preparations and implementation shall take into account forthcoming recommendations from SAGE and be in consultation with Alliance partners. Approval will be subject to sufficient additional funding being available and Board endorsement of moving this forward outside the timing of the VIS process and the Board will note that there may need to be changes to GAVI policies which would need to be approved by the Board or the Executive Committee.¹

4 Risk and Financial Implications – Update

- 4.1 Estimates of impact are a major driver of prioritisation in the VIS and have been developed in consultation with technical institutes and validated by an Independent Expert Committee. For some vaccines the evidence base for the addressable disease burden and for vaccine effectiveness is incomplete. For those vaccines where estimates of impact are particularly uncertain, the Secretariat will continue to assess new data over the coming months and update the estimates as needed. If such revisions lead to substantial changes (ie a change from relatively high to low impact or vice versa), the shortlist of priority vaccines to be considered in phase II of the VIS process will be updated accordingly.
- 4.2 Risks and financial implications related to an accelerated decision on IPV investment are addressed in Doc 07.

¹ As mentioned in Section 2.6, a possible GAVI investment in IPV is the subject of Doc 07.



Report to the Programme and Policy Committee

29-30 April 2013

Subject: GAVI's Vaccine Investment Strategy

Report of: Nina Schwalbe, Managing Director, Policy and Performance

Authored by: Judith Kallenberg, Aurelia Nguyen

Agenda item: 07

Category: For Decision

Strategic goal: SG1 - Underused and new vaccines

Section A Overview

1 Purpose of the report

- 1.1 In 2008 the GAVI Alliance Board endorsed a Vaccine Investment Strategy (VIS) for 2009-2013 and requested that the Secretariat re-evaluate the vaccine landscape in 2013 in order to explore additional areas for GAVI investment.
- 1.2 In October 2012 the Programme and Policy Committee (PPC) provided guidance on the proposed two-phase process for developing the VIS in 2013.
- 1.3 This report presents an overview of the completed phase I of the VIS process, including analyses done for all vaccines under consideration against a comprehensive set of evaluation criteria. It requests a PPC recommendation on the prioritisation approach and related vaccine shortlist for decision by the GAVI Board at its June meeting. The Secretariat would then proceed with further analyses in phase II and, in consultation with the Technical Consultation Group and Independent Expert Committee, request a PPC recommendation in September for future vaccine priorities additional to the current GAVI portfolio for eventual Board consideration in November.

2 Recommendations

The Secretariat requests the PPC to:

2.1 Recommend to the Board that it:

- (a) Endorses the evaluation criteria set out in Table 1 in Doc. 07 for consideration in the Vaccine Investment Strategy (VIS) process;

- (b) **Option 1:** Decides to narrow the choice of possible vaccine investment options (in addition to GAVI's current portfolio) for further analysis in Phase II by prioritising vaccines based on health impact (mortality and morbidity). As modelled in Phase 1 of the VIS, influenza (for maternal immunisation), malaria and rabies vaccines are in the top tier of health impact outcomes; **OR**

Option 2: Decides to narrow the choice of possible vaccine investment options (in addition to GAVI's current portfolio) for further analysis in Phase II by prioritising vaccines based on health impact (mortality and morbidity), epidemic potential, and value for money (procurement cost per death averted). As modelled in Phase I of the VIS, influenza (for maternal immunisation), malaria and rabies vaccines are in the top tier of health impact outcomes; cholera and yellow fever vaccines are included on the basis of epidemic potential and value for money outcomes. Dengue, meningitis (serogroups CYW) and measles, while diseases with epidemic potential, are excluded from further analysis because of a relatively high cost per death averted (low value for money) of the modelled strategy; and

- (c) Decides to also include for further evaluation in Phase II a potential GAVI investment in Inactivated Polio Vaccine as a contribution to polio eradication.

3 Executive Summary

- 3.1 In November 2013 the GAVI Board will consider a new Vaccine Investment Strategy for the period 2014-2019. The objective of the VIS is to enable upfront, evidence-based decisions about GAVI's future vaccine investments in order to align planning by countries, industry and donors for the introduction of new, priority vaccines. Existing vaccines and vaccines in development with an anticipated licensure date by 2019 are being considered.
- 3.2 As a starting point, WHO has conducted a vaccine landscape analysis and provided GAVI with a list of 15 diseases for which vaccines are available or expected to be licensed by 2019: cholera, dengue, DTP (booster), EV71, hepatitis A, hepatitis B (birth dose), hepatitis E, seasonal influenza, malaria, measles, meningococcal disease, mumps, poliomyelitis, rabies, and yellow fever.
- 3.3 Following an initial analysis by the Secretariat, no further assessment was undertaken for mumps, EV71 and DTP (booster) vaccines. An Independent Expert Committee (IEC) supported the Secretariat's proposal to exclude these from detailed analysis in phase I because of very limited data on disease burden and high probability of low vaccine impact relative to other vaccines being evaluated.
- 3.4 To facilitate a multi-faceted evaluation of the remaining twelve vaccines under consideration, the Secretariat developed 18 evaluation criteria

grouped in four categories: health impact, additional impact considerations, implementation feasibility, cost and value for money. These evaluation criteria were validated through consultations with GAVI stakeholders. The Secretariat has assessed all vaccines against these criteria. Quantitative and qualitative scores have been given a red/yellow/green colour code based on pre-defined thresholds to show how the vaccine performs (poorly/neutrally/well) against each criterion relative to the other vaccines. Results have been mapped in vaccine 'scorecards' to facilitate cross-disease analyses. Different evaluation criteria may be applied in phase I and phase II to guide vaccine prioritisation.

- 3.5 Based on feedback from stakeholder consultations and guidance by the IEC, health impact (deaths/cases averted) is proposed as the primary strategic focus for prioritising potential vaccine investments for further evaluation in Phase II. Value for money and the epidemic potential of vaccine-preventable diseases, parameters that are not captured by estimates of deaths and cases averted alone, are also considered to guide prioritisation.
- 3.6 Based on individual vaccine evaluations against the criteria, and on the broad prioritisation approach described above, the Secretariat proposes two options for a strategic direction to guide prioritisation of vaccines for further analysis in phase II (see section 2). In addition, the Secretariat proposes to include a potential GAVI investment in inactivated polio vaccine (IPV) for further evaluation in Phase II, as a contribution to polio eradication.

4 Risk implication and mitigation

- 4.1 Risks related to the proposed approach for prioritising vaccines for further analysis in phase II include:
 - (a) A focus on health impact considerations may not reflect the views or interests of all GAVI Alliance stakeholders. This risk has been mitigated by actively engaging GAVI stakeholders in the process through consultations to inform evaluation criteria and the relative importance of these for prioritisation.
 - (b) Incorrect or incomplete inputs into vaccine analyses could distort vaccine evaluation outcomes. This risk has been mitigated by ensuring extensive expert guidance on data sources, analysis methods and assumptions, through individual expert consultations and through the Independent Expert Committee review. Diseases with limited or poor quality burden data have been excluded from consideration. The VIS presents an opportunity for highlighting a research agenda for these diseases to ensure that the potential value of vaccines against these diseases is better understood in future considerations by GAVI or others.

- 4.2 By including additional vaccines in GAVI's future portfolio, the VIS could increase the risk that countries introduce vaccines faster or in larger numbers than systems are ready to absorb. This could lead to a burden on health systems and inefficient use of resources. Two evaluation criteria draw attention to such considerations: the criteria on 'ease of programmatic integration' and 'in-country operational cost'. Scoring of vaccines against these criteria is based on vaccine delivery routes (e.g. routine or campaign delivery), alignment with other vaccines schedules and changes required in health worker practice, amongst other factors, as described in the presentation on scoring methodologies available on myGAVI. In phase II, a refined analysis of in-country operational costs will be conducted, as well as a fiscal space analysis. Future application guidelines, developed prior to opening a new funding window, would include country readiness requirements. Beyond the Vaccine Investment Strategy, the Secretariat will also assess the feasibility of a health technology assessment tool, in particular for use by graduating countries.
- 4.3 Following decisions by the Board in November, significant changes to the assumptions underlying VIS decisions may occur. For example, changes in vaccine efficacy and/or burden data, changes in product development timelines and outcomes of clinical trials, price or volume changes relative to the assumptions for cost estimates, and funding shortfalls. These risks will be mitigated through a complete review of assumptions by the Secretariat prior to opening a funding window.

5 Financial implications: Business plan and budgets

- 5.1 The decision to prioritise vaccines for further evaluation in phase II does not constitute an investment decision.
- 5.2 Final decisions in November 2013 on potential new vaccine investments will have financial implications relating to GAVI's vaccine support programmes. Annex G presents preliminary cost estimates for all vaccines considered in phase I, over the period 2015-2030. Updated cost estimates for vaccines prioritised in November are expected to be lower, when demand forecasts are integrated to include existing commitments and phasing of potential new vaccine introductions. The opening of any new funding window will be contingent on successful outcomes of the upcoming resource mobilisation round.

Section B Content

1 Background

- 1.1 The objective of the VIS is to enable upfront, evidence-based decisions about GAVI's future vaccine investments in order to align planning by countries, industry and donors for the introduction of new, priority vaccines. The approach helps pre-empt first-come-first-serve decisions by GAVI for individual vaccines becoming available at different times in this time period. In addition, predictable programming helps countries

understand what vaccines may and may not be feasible to introduce and inform planning by Ministries of Health and Finance. The VIS also gives vaccine manufacturers a clear signal of GAVI's intention to procure certain products, which could help accelerate development timelines and boost investments in production capacity. Finally, cost estimates of future implementation of vaccines prioritised in the VIS provide donors with a clear forecast of GAVI's future financial needs. Of note, emerging policy guidance from the World Health Organization (WHO) will be included in any recommendation to the Board and in future implementation guidelines.

- 1.2 The 2008 Vaccine Investment Strategy process led to the GAVI Board's decision to prioritise meningitis A, Japanese Encephalitis (JE), typhoid, human papillomavirus (HPV), and rubella vaccines for addition to GAVI's portfolio. Further, the Board expressed its intention to monitor the development of malaria and dengue vaccines. Cholera and rabies were shortlisted, but eventually not prioritised for investment as they compared less favourably to other shortlisted vaccines.

2 Scope

- 2.1 WHO conducted an initial vaccine landscape analysis and provided GAVI in December 2012 with a list of diseases for which vaccines are available or expected to be licensed by 2019: cholera, dengue, DTP (booster), EV71 (Hand, Foot, Mouth disease), hepatitis A, hepatitis B (birth dose), hepatitis E, seasonal influenza, malaria, meningococcal disease, mumps, poliomyelitis, rabies and yellow fever. GAVI's current commitments to support vaccines on an ongoing basis (e.g. pentavalent, rotavirus, pneumococcal, HPV, JE, typhoid, and rubella vaccines) are not revisited. However, investments in expanded support for vaccines already in GAVI's portfolio are considered in those instances where GAVI's initial support was limited in scope and where an expansion of scope could be considered in accordance with WHO recommendations. For example,

- (a) An expansion of the country scope and/or target population in the original GAVI commitment (measles, yellow fever)
- (b) An expansion of support for vaccines that target additional serogroups (meningococcal disease)
- (c) Support for complementary vaccination strategies (DTP booster, Hepatitis B birth dose).

- 2.2 Vaccines primarily indicated for emergency response or biosecurity purposes (e.g. SARS) or that are too early in development and have an extremely low likelihood of licensure or WHO prequalification by 2019 (e.g. Streptococcal disease groups A and B, HIV/AIDS and RSV) were not considered. The latter remain of high interest to GAVI, and vaccine development will be monitored as part of market shaping activities. The WHO landscape analysis initially included tuberculosis because there was a possibility that the most advanced vaccine in the pipeline (MVA85A) would be licensed by 2019. However, after the recent failure of the infant

IIB trial, adult trials are likely to be discontinued. In coordination with WHO, tuberculosis was therefore removed from the list of vaccines under consideration.

- 2.3 Following initial analyses and expert consultations, the Secretariat excluded DTP booster, mumps and EV71 from further consideration based on low or unknown (addressable) disease burden. The potential impact of DTP booster vaccination is likely to be relatively low and cannot be confidently modelled because of lack of evidence on waning protection (of whole cell pertussis vaccines) and therefore addressable burden. Enterovirus 71 is a cause of Hand, Foot and Mouth disease, which is generally a mild disease with low case fatality rates. Outbreaks have been reported in two GAVI-eligible countries (Vietnam and Cambodia), but reported data are incomplete and inconsistent. There is very limited burden data for mumps, which is generally a mild disease, and mumps vaccines have a high probability of low impact relative to other vaccines under consideration. The remaining twelve vaccines have been analysed in detail as described in section 3 below.

3 Process

- 3.1 The VIS is being developed in two phases. The first phase began with a 'long list' of potential vaccine investment options and ends with the Board's decision in June 2013 on a strategic focus for the VIS and a related narrowing of vaccine options for further consideration. In the second phase, potential GAVI investments in vaccines 'shortlisted' as a result of the strategic direction chosen will be further evaluated to inform a final decision by the Board in November 2013 on selected vaccines for addition to GAVI's portfolio in 2014-2019.
- 3.2 To facilitate a multi-faceted evaluation of the twelve vaccines under consideration, the Secretariat developed eighteen **evaluation criteria** grouped in four categories: health impact, additional impact considerations, implementation feasibility, cost and value for money (see table 1 below). They build on criteria considered in the 2008 process and have been vetted with GAVI Alliance stakeholders through consultations¹. The criteria provide a perspective on the cost and health impact outcomes of potential GAVI investments (quantitative), and on relevant disease and vaccine characteristics (quantitative and qualitative). The Secretariat has analysed all vaccines against these criteria. Quantitative and qualitative scores have been given a red/yellow/green colour code based on pre-defined thresholds to show how the vaccine performs (poorly/neutrally/well) against each criterion relative to the other vaccines. Results have been mapped in vaccine 'scorecards' to facilitate cross-disease analyses. Detailed disease presentations, including vaccine 'scorecards' are available on myGAVI. Also available on myGAVI is a presentation detailing the methodology for scoring vaccines against each indicator.

¹ The criteria are also aligned with the criteria used in GAVI's prioritisation mechanism, see paper #9 for this meeting.

Table 1: Vaccine evaluation criteria and indicators

Category	VIS Criteria	Phase I Indicator
Health impact	Impact on child mortality	U5 future deaths averted, 2015 – 2030
		U5 future deaths averted per 100,000 vaccinated population
	Impact on overall mortality	Total future deaths averted, 2015 – 2030
		Total future deaths averted per 100,000 vaccinated population
	Impact on overall morbidity	Total future cases averted, 2015 - 2030
		Total future cases averted per 100,000 vaccinated population
Additional impact considerations		Long-term sequelae (yes / no)
	Epidemic potential	Disruptive epidemic potential of disease (yes / no)
	Global or regional public health priority	Presence of global / regional (UN) resolution on elimination or eradication (yes / no)
	Herd immunity	Herd immunity threshold (above or below 70%)
	Availability of alternative interventions	Current use of alternative interventions for effective disease control (prevention and treatment) and potential for scale up (yes / no)
	Socio-economic inequity	Disproportionate impact on poor (yes / no)
	Gender inequity	Disproportionate impact on one gender (yes / no)
Implementation feasibility	Disease of regional importance	Burden concentrated in a subset of GAVI countries within same region (yes / no)
	Capacity and supplier base	Capacity to meet GAVI demand (<75% / 75-100% / >100%) and # of manufacturers by 2020 (1 / 2 / 3+)
	GAVI market shaping potential	GAVI demand as % of global demand (<10% / 10-25% / >25% by volume)
	Ease of supply chain integration	Packed volume (cm3) compared to benchmarks
	Ease of programmatic integration	Alignment with other vaccine schedules (fully / partially / not aligned) and significant change in health worker practices/behavior required (yes / no)
	Vaccine efficacy and safety	Vaccine efficacy (above or below 50%, as defined by clinical endpoints) and safety (evidence or no evidence of causal link with severe adverse events)
Cost and value for money	Vaccine procurement cost ¹	Total procurement cost to GAVI and countries, 2015 – 2030
	In-country operational cost	Incremental in-country operational cost per vaccinated person (high / medium / low)
	Procurement cost per event averted ²	Procurement cost per death / case averted

1. Procurement cost includes vaccine, syringe, safety box, and freight 2. Scoring based on cost per future death averted

- 3.3 The complete set of evaluation criteria forms a framework to help facilitate prioritisation. Selected criteria may be given priority based on different strategic perspectives. In phase I, the Secretariat recommends using the criteria on health impact (option 1), possibly combined with the criteria on epidemic potential and value for money (option 2) for prioritising vaccines for further analysis in phase II. In phase II, vaccines shortlisted as a result of the chosen strategic focus would be further ranked on the basis of these and potentially other criteria, based on guidance by the TCG, the IEC and findings from stakeholder consultations.
- 3.4 As a starting point for the analyses, potential **vaccination strategies** for GAVI-eligible countries were identified based on disease epidemiology, vaccine product profiles, expert input and WHO recommendations where they exist. For example, for a potential GAVI investment in (seasonal) influenza vaccines, per WHO guidance in the 2012 position paper, vaccination of pregnant women was considered as the investment strategy for consideration in the VIS. Similarly, post-exposure prophylaxis was identified for the evaluation of a potential investment in rabies vaccines. Annex A summarizes the vaccination strategies identified to model and evaluate the cost and impact of each vaccine, including delivery route, target population and vaccination schedule. The individual disease presentations on MyGAVI provide further details on the rationale for

modelled strategies. For certain vaccines, multiple vaccination strategies were analysed, and for each vaccine a base case scenario was selected. All strategies have been developed for modelling purposes, to be able to provide the PPC with comparable estimates across vaccines. If GAVI were to prioritise any of these vaccines, actual implementation strategies would be guided by potential additional guidance received from WHO's Strategic Advisory Group of Experts and other WHO expert bodies.

- 3.5 A **demand forecast** has been developed for each vaccine to assess the cost and health impact implications of potential future GAVI investments. 2015 was assumed as the first year of potential introduction and demand was forecasted through 2030. Known or estimated endemicity determines which countries introduce a vaccine in the forecast, while the timing of introduction is driven by historical vaccine introduction patterns. Annex A lists key forecasting inputs for each vaccine, including the vaccination strategies currently identified as the 'base case' for VIS analyses.
- 3.6 **Price forecasts** were developed based on existing prices where available or proxies from other vaccines with similar technologies, adjusted for estimated manufacturer cost structures and capacities. An estimated, projected price (averaged over multiple products where relevant) was combined with the demand forecast to produce annual and overall cost estimates.
- 3.7 The potential health impact of vaccines (estimated deaths and cases averted) is a key input for the VIS prioritisation process. Where existing models were available (e.g. malaria, cholera, yellow fever), the Secretariat worked with the relevant experts or expert groups to generate **impact estimates**, ensuring minimum bias and maximum consistency across vaccines. For those vaccines without existing models, a standard model was built to estimate impact across vaccinated cohorts, based on future death and case rate estimates, and vaccine efficacy.
- 3.8 Analyses were developed in close consultation with a wide range of vaccine and disease experts, technical partners and manufacturers. Annex H presents a full list of institutions consulted. Detailed disease presentations with all analysis outputs, forecasting and impact modelling assumptions are available on MyGAVI. Annex C presents a summary of key analysis outputs for all vaccines under consideration. Following a competitive bidding process, the Boston Consulting Group was contracted to provide analytical support to the process.
- 3.9 A Technical Consultation Group (TCG) has been established to provide input into the process and methodologies used during the VIS process. The TCG consists of representatives of GAVI Board constituencies with expertise in epidemiology, health impact, health financing, immunisation programmes and vaccine manufacturing. Annex D lists the members of the TCG.
- 3.10 An Independent Expert Committee (IEC) has been established to validate VIS data inputs and vaccine analysis methods, including modelled

vaccination strategies, impact modelling assumptions and methods for scoring vaccines against VIS criteria. Members serve in their personal capacity and have expertise in a variety of areas including but not limited to epidemiology, immunisation, vaccine development, infectious disease control, health systems, economic analysis and health financing. Annex E lists the members of the IEC, which is chaired by Professor Robert Black (Chairman, Johns Hopkins Bloomberg School of Public Health). The Chair's summary of the IEC's review of phase I analyses is included as Annex B.

- 3.11 In addition to expert consultations, GAVI stakeholders are being consulted throughout the process to inform key components of the VIS through meetings and surveys distributed at relevant global and regional meetings (e.g. GAVI Partners Forum, EPI Managers' meetings, SAGE, World Health Assembly). These consultations have so far focused on generating and validating vaccine evaluation criteria, understanding country-level public health priorities and implementation feasibility of different vaccines and vaccination strategies. Consultations are also used as an opportunity to share information about the VIS process and provide updates. A summary of country consultation findings can be found on myGAVI.
- 3.12 GAVI is committed to transparency with regards to the VIS process and outcomes. Information about the project, analyses and consultation findings will be shared with relevant stakeholders. Selected documents will be made public following the Board meetings in 2013. Confidential information such as vaccine price projections and manufacturers' production capacity plans will not be shared publicly.

4 Strategic options

- 4.1 No single algorithm or weighting of criteria can do justice to the diverse considerations reflected in the eighteen evaluation criteria. To enable careful and objective consideration of the attributes of a disease and its related vaccine(s) that are relevant for prioritisation, the Secretariat proposes a stepwise approach to determine strategic priorities.
- 4.2 First, based on feedback from stakeholder consultations and guidance by the Independent Expert Committee (IEC), health impact is proposed as the primary strategic focus for prioritising potential vaccine investments for further evaluation in Phase II. Three separate criteria were developed to capture different aspects of the potential health impact of vaccines:
 - (a) Impact on child mortality (under 5 year old deaths)
 - (b) Impact on overall mortality (deaths)
 - (c) Impact on morbidity (cases)

For each vaccine, the health impact implications of GAVI's potential investment has been analysed in terms of the total projected number of deaths or cases averted over the period 2015-2030, as well as the number of deaths or cases averted per 100,000 persons vaccinated. Annex F presents the ranking of vaccines under consideration against these health

impact criteria. Under currently modelled vaccination scenarios, influenza, malaria and rabies are in the top tier of all three health impact outcomes.

- 4.3 Second, stakeholder feedback and IEC guidance further indicated that vaccines for diseases with disruptive epidemic potential may not score high on overall impact, but could play an important role in reducing the risk of outbreaks and therefore merit special consideration. Diseases with high epidemic potential include cholera, dengue, polio, malaria, measles, meningitis and yellow fever.
- 4.4 Third, the TCG and IEC considered value for money (reflected as cost per death averted) to be an important criterion to take into account for any prioritisation decisions. Vaccine investments with the lowest cost per death averted (high value for money) on the basis of modelled vaccination strategies include rabies, hepatitis B, yellow fever, influenza, malaria, cholera and hepatitis E.
- 4.5 Based on the above considerations, and following review by the IEC, the Secretariat proposes two options for a strategic direction to guide prioritisation of vaccines for further analysis against evaluation criteria in phase II, as outlined in section A.2. In addition, recognizing the unique value of IPV introduction as a critical component of polio eradication, the Secretariat proposes to include a potential GAVI investment in IPV for further evaluation in Phase II. This is in light of the Board's decision in December 2012 to play a complementary role to the Global Polio Eradication Initiative (GPEI), which is further explored in the PPC paper #05 for this meeting on GAVI's role in the polio eradication effort.
- 4.6 Repeated measles campaigns or Supplementary Immunisation Activities (SIAs) in children under five years of age are supported by the Measles Rubella Initiative (MRI). GAVI exceptionally supports measles SIAs in six high risk countries in children under five years of age, for a limited period of time. The Secretariat has analysed the incremental impact of an investment in expanding the age cohort for measles campaigns in all GAVI-eligible countries as a potential strategy contributing to measles elimination².
 - (a) The baseline in this analysis assumes that campaigns in children under five are funded by the MRI and implemented as planned³.
 - (b) Based on expert guidance, the base case strategy modelled for the VIS increases the age range to 15 years in one out of every three campaigns.
 - (c) This 'top-up' investment to accelerate elimination results in marginal additional impact on mortality (i.e. twelve thousand incremental deaths averted in 2015-2030).

² The WHO's SAGE is expected to issue guidance on the value of 'repeat catch-up' campaigns targeting older children (9M-<15Y) in 2013.

³ Based on an MRI forecast of measles and measles/rubella SIAs in 2013-2020 provided to GAVI by WHO on 31 March 2013

As a standalone investment this strategy does not compare favourably to the other vaccine investments considered in the VIS. Therefore, the Secretariat is not proposing at this stage to explore potential future contributions to measles beyond the current scope of countries agreed by the Board. This recommendation may be reviewed following SAGE recommendations on the appropriate strategies for measles SIAs, as well as resources raised for the MRI.

- 4.7 In phase II, cost and value for money will be important considerations to guide investment decisions, alongside other prioritised criteria indicated during consultations. Annex G presents a ranking of cost and value for money outcomes for the vaccines under consideration, based on currently modelled strategies. Other criteria that may be considered in phase II include the availability of alternative interventions, impact on gender inequity and other criteria within the proposed vaccine evaluation framework that consultations may highlight.

5 Next steps

- 5.1 In phase II of the VIS process the Secretariat will develop refined and additional vaccine analyses and evaluate investment portfolio options.
- (a) Impact and cost analyses for vaccines prioritised in phase I will be further refined based on updated information and expert guidance. An updated forecast will likely decrease the absolute impact and cost estimates for VIS vaccines when demand forecasts are integrated to include existing commitments and phasing of potential new vaccine introductions.
 - (b) Additional analysis will be carried out to assess the fiscal space available in countries to increase commitments to immunisation programmes whilst ensuring sustainability.
 - (c) Additional analysis will be carried out to refine incremental in-country operational costs for vaccine delivery, as well as to assess broader health system implications.
 - (d) Potential synergies between different vaccines and linkages with other disease control initiatives will also be assessed, as well as economic impact of vaccines where this is available from published sources. Depending on the vaccines carried forward in phase II, robust and comparable assessments of future DALYs averted may not be feasible within the current project scope.
 - (e) Analyses will be benchmarked against existing GAVI commitments (for example to compare the cost per death averted of a VIS investment with that of currently GAVI-funded vaccines).

- (f) Of note, the analysis of a number of shortlisted vaccines in phase II does not indicate final inclusion of any or all of these vaccines for investment decisions in November. In addition, some vaccines may no longer be in scope for the VIS during phase II due to delays in development or failure to pass clinical milestones.

5.2 The anticipated timeline for phase II of the VIS process is:

- (a) Q2 2013: continued stakeholder consultations; development of the analytical approach for vaccine-specific and portfolio level analyses to be conducted in phase II
- (b) Q3 2013: expert consultations; vaccine and portfolio level analyses for phase II; TCG guidance; IEC review of analyses; country consultations
- (c) Q4 2013: PPC guidance on VIS board recommendation.

5.3 Based on recommendations from the PPC, in November 2013 the Board will consider a VIS portfolio that adds selected vaccines to GAVI's future programme based on a comprehensive analysis of impact and cost implications. Indicative cost estimates will be presented in the context of GAVI's overall financials.

5.4 After the board's decision in November, newly prioritised vaccines would be incorporated in GAVI's vaccine support programmes following successful resource mobilisation and development of implementation guidelines:

- (a) Resource requirements for vaccines prioritised in the VIS will be reflected in GAVI's long term funding strategy and as part of future fundraising efforts, including the upcoming pledging round for 2015-2019 (introductions of VIS vaccines would not occur before 2015, with the possible exception of IPV in support of the Polio Endgame Strategy).
- (b) Prior to opening a funding window, the GAVI Secretariat will conduct a complete review of vaccination strategies and other key assumptions, and will develop implementation strategies and application guidelines in collaboration with technical partners, based on updated analyses and the most recent policy guidance from WHO.

Section C Implications

1 Impact on countries

1.1 Through the VIS process, countries get long-term visibility of the new vaccines prioritised for future support by the GAVI Alliance. The VIS process also provides an opportunity to share key information about the vaccines under review - such as expected product profiles, estimated

health impact, cost, supply availability and programmatic challenges. This could help inform countries' decision making linked to the desirability, affordability and timing of new vaccine introduction and support long-term planning.

- 1.2 The financial impact on countries and overall fiscal space to support additional vaccines will be analysed as part of the VIS process in phase II. As noted above, GAVI will also aim to support the development of a health technology investment tool to assist countries, in particular those which may graduate, with decision making.

2 Impact on GAVI stakeholders

- 2.1 The VIS is likely to affect all GAVI stakeholders and will require additional investment in all areas of GAVI's work including vaccine introduction support, monitoring and evaluation, and market shaping.
- 2.2 The VIS will enable predictable programming and help align planning around new vaccine introduction by countries, industry, technical and implementing partners, as well as GAVI donors.

3 Impact on Secretariat

- 3.1 The VIS project is included in the 2013 business plan and budget. In addition to resources allocated from existing headcount, one full time senior specialist was recruited for the duration of the project.
- 3.2 The number of vaccines shortlisted for further evaluation in phase II will impact the quality and comprehensiveness of analyses that can be carried out with currently allocated resources.

4 Legal and governance implications

- 4.1 There are no legal or governance implications resulting from the recommendations in this report.

5 Consultation

- 5.1 The Secretariat has conducted extensive consultations with experts and expert groups to inform key components of the analyses. In addition, broader consultations have been conducted with GAVI stakeholders, both through the TCG as well as through surveys distributed at relevant global and regional meetings. These consultations have focused on validating vaccine evaluation criteria, understanding country-level public health priorities and implementation feasibility of different vaccines and vaccination strategies. The following consultations were undertaken in phase I:

- (a) Stakeholder consultations to develop vaccine evaluation criteria were conducted in December 2012 at the GAVI Alliance Partners Forum, and at various regional meetings. Feedback was collected through dedicated sessions and the administration of a questionnaire which elicited 116 responses. This consultation largely confirmed the relevance of the proposed evaluation criteria, with health impact being highlighted as most important.
- (b) Country consultations on public health priorities and the potential role of vaccines in addressing those priorities were held in February/March 2013 targeting country delegates and partners at different regional meetings. Feedback was received in dedicated sessions and through the administration of a second questionnaire which elicited 89 responses from 33 GAVI-eligible countries. Preliminary findings – predominantly from the AFRO region – highlight malaria, polio and measles as public health priorities, amongst others, while vaccines against hepatitis E, dengue and influenza were given low priority. Consultation participants cited cold chain and logistics, as well as sustainable vaccine financing as challenges for new vaccine introduction. Findings from this consultation round will help inform the focus of further analyses in phase II.
- (c) Individual consultations with vaccine/disease experts, Product Development Partnerships and technical partners, as well as manufacturers have helped inform key components of the analysis. Annex H presents a full list of groups consulted.

5.2 A summary of the different stakeholder consultations is available on myGAVI.

5.3 Consultations will continue in phase II and will focus on validating vaccine priorities and informing integrated and updated demand forecasts, as well as provide further understanding of potential challenges related to new vaccine introduction.

6 Gender implications

6.1 As part of the vaccine scorecards the potential for a disproportionate impact of the disease on one gender (higher prevalence and/or suffering) has been assessed and reflected for each disease.

Section D Annexes

- A. Base case vaccination strategies and forecasting inputs for VIS modeling purposes
- B. Independent Expert Review – Chair’s Summary
- C. Summary of key analysis outputs for vaccines under consideration (2015-2030)
- D. Members of the Technical Consultation Group for the Vaccine Investment Strategy 2013
- E. Members of the Independent Expert Committee for the Vaccine Investment Strategy 2013
- F. Summary of health impact outcomes by vaccine
- G. Summary of cost and value for money outcomes by vaccine
- H. Expert consultations

Available on MyGAVI:

- 12 diseases presentations
- Summary of vaccine scorecards
- Methodology for scoring vaccines against indicators
- Standard demand forecasting and cost assumptions
- Overview of stakeholder consultations

A. Base case vaccination strategies and forecasting inputs for VIS modeling purposes

Disease	# of Countries	Delivery strategy	Target population (catch up / routine)	Doses (Interval between doses)	First intro year	Demand coverage analogue
Cholera	19	Campaign (every 3 years)	1-15y (50% of high risk population)	2 (0, 2 weeks)	2015	MSIA
Dengue	7	Campaign (x1) / Routine	2-15y / 2y	3 (0, 6, 12 months)	2018	DTP2 (25% discount)
Hepatitis A	4	Routine	12m	1	2015	MCV1
Hepatitis B	36	Routine	Infants	1 (at birth)	2015	Institutional births
Hepatitis E	10	Routine	10y women	3 (0, 1, 6 months)	2016	DTP2 (25% discount)
Influenza	48	Routine	Pregnant women	1 (at first antenatal visit)	2015	TT1 (25% discount)
IPV	56	Routine	Infants	1 (with DTP3)	2015	DTP3
Malaria	34	Campaign (x1) / Routine	5-18m / Infants	3 (0, 4, 8 weeks)	2017	DTP2 (25% discount)
Measles¹	51	Campaign (every 6-12 years)	5-15y	1	2015	100% of target population
Meningitis CYW	26	Routine	9m	2 (0, 3 months)	2015	MCV1
Rabies	47	PEP ² (incremental)	Untreated victims	8 (2 per visit, 4 visits total)	2015	95% of target ³
Yellow fever	9	Campaign (x1)	>1y in high risk population	1	2016	100% of target population

1. Considers incremental impact only of expanding every third campaign to cover the 5-15y age group 2. Post exposure prophylaxis 3. Treatment seeking behavior captured in target population modeling

Detailed demand forecasting and impact modelling assumptions are documented in the individual disease presentations available on MyGAVI.

B. Independent Expert review – Chair's summary

Independent Expert Committee for the GAVI Vaccine Investment Strategy

27-28 March 2013, Washington DC

Members attending: Dr. Robert Black (Chair), Dr. Jane Achan, Dr. Raj Bahn, Dr. Fred Binka, Dr. Kalypso Chalkidou, Dr. Melinda Moree, Dr. Helen Rees, Dr. Anne Schuchat

GAVI Secretariat: Aurelia Nguyen, Judith Kallenberg, Emily Serazin (Boston Consulting Group)

Chair's summary

Members of the IEC were asked to declare any conflicts of interest. Fred Binka declared his involvement in supporting RTS,S trial sites. Other members did not declare any current conflicts of interest in relation to the vaccines under consideration.

The IEC commends the GAVI Secretariat for the quality of the materials presented. The scope of disease- and vaccine-specific information, the depth of analyses and transparency of assumptions constitute a robust foundation for evaluation of individual vaccine and portfolio opportunities. The VIS 2013 analysis represents a significant improvement over the work done in 2008.

The IEC recognized that all vaccination strategies have been developed for modelling purposes, to be able to generate comparable estimates across vaccines. Current advice and future prioritization decisions will be conditional on guidance from WHO's Strategic Advisory Group of Experts, WHO pre-qualification and other relevant outstanding review processes.

2013 VIS scope

- The IEC agreed that no further analysis of the DTP booster, EV71 and mumps vaccines should be undertaken following an initial assessment by the Secretariat. The reasons to exclude these from detailed cross-disease evaluation in phase I include a relatively low disease burden and uncertainty about the addressable burden.
- The Secretariat clarified that although typhoid (prioritized in the VIS 2008) is built into GAVI's projected ongoing vaccine support programs and will not be revisited in the 2013 VIS process.

Vaccine evaluation criteria

- The IEC suggested including vaccine safety as a criterion in the vaccine 'scorecards' and splitting vaccine efficacy and herd immunity into two separate criteria. The IEC also suggested removing the indicator related to controlled temperature chain since this reflected potential future improvements rather than the current status of products. Otherwise, the committee felt that the framework of evaluation criteria is complete. It suggested some minor clarifications in the description of indicators related to alternative interventions and diseases of regional importance.
- The IEC endorsed the approach for 'scoring' vaccines against criteria which generates a helpful map of relevant implications and contextual factors for consideration for each vaccine. It noted that, for an initial prioritization in phase I, the Board may want to articulate a strategic direction based on prioritizing one or two of these criteria (e.g.

impact on mortality) in addition to value for money considerations, rather than to apply weights to each individual criterion.

- The IEC felt that programmatic feasibility criteria should not be used to exclude any vaccine.

Cross-vaccine prioritization

- The IEC selected impact on mortality as the most important criterion, followed by cost per death averted (value for money).
- Based on this decision framework, the IEC recommended that the vaccines identified as having the highest impact on mortality (currently identified as hepatitis B (birth dose), influenza (seasonal), malaria and rabies vaccines according to the vaccination strategies presented during the meeting) be considered for further analysis in phase II.
- Further discussions on cholera and yellow fever vaccines showed a more nuanced balance of pros and cons for further consideration in phase II.
- Vaccines with low mortality (currently identified as Dengue, hepatitis A, hepatitis E and conjugate meningitis ACWY vaccines according to the vaccination strategies presented during the meeting) were considered low priorities and the IEC recommended not taking these forward for further detailed analysis in phase II.
- The committee believed a revised analysis for measles would be required in order to evaluate the incremental benefit and cost of a measles SIA strategy (over and above campaigns already planned by the Measles Rubella Initiative). However, regardless of the analysis done the committee questioned if additional support for measles control was a priority within the mandate of GAVI.
- The IEC suggested that the rationale for further consideration of IPV as part of phase II was strong within the context of the global polio eradication strategy. Further details on the rationale for these categorizations can be found below.

Polio

The IEC reviewed the proposed investment in IPV administration in line with the Global Polio Eradication Initiative Endgame Strategy. The committee concluded that GAVI's involvement in polio eradication merits separate consideration outside the proposed evaluation framework. IPV does not 'compete' with other vaccines given the unique objective of this investment and this should be made explicit in the decision. The IEC noted the following items for consideration by the GAVI Board:

- The decision to support IPV is time-sensitive with eradication planned and expected for 2015-2020. Unlike other potential investments, it cannot be postponed or revisited in 5-10 years.
- GAVI's comparative advantage in supporting polio eradication and shaping the IPV market needs to be viewed in light of other stakeholders and potential funding sources.
- Investment in IPV could be seen as a deviation of GAVI's mission around catalyzing access to new vaccines.
- There may be an opportunity cost for other vaccines associated with supporting widespread IPV introductions in 2015-2016.
- The Board should carefully consider the possible 'legacy' of an investment in IPV if eradication timelines change.

Malaria

The IEC reviewed a "base case" vaccination strategy (for modelling purposes) focused on vaccinating children at 6, 10 and 14 weeks in the EPI schedule. The committee discussed the

validity of model inputs and assumptions, including transmission intensity data (as modelled in the Malaria Atlas Project), vaccine efficacy (31.3%), duration of protection and direct vs. indirect mortality. The committee also reviewed the impact estimates for an alternative scenario of vaccinating 5-17 month olds, in which vaccine efficacy has been shown to be higher. Given the significant disease burden and possible high impact of a vaccine, the IEC advised that the malaria vaccine would be of strong interest for further evaluation. The Committee also felt there would be considerable market-shaping potential for GAVI. It noted however the significant uncertainties around efficacy and duration of protection of the leading vaccine candidate in particular, and suggested any decision would need to consider this carefully. Clinical trial results will continue to emerge over the coming years and should be monitored closely to better understand efficacy and the waning of immunity over time, and the implications for the benefits of introducing this vaccine in GAVI-eligible countries. For impact modeling in phase II, the IEC suggested using updated estimates of transmission intensity (updated from the current 2010 estimates), varying trends of coverage of alternative interventions, and to also explore a possible vaccination strategy of campaigns without routine immunization.

Yellow Fever

The IEC supported the "base case" vaccination strategy of one-off, mass campaigns in selected countries based on a WHO risk assessment. The IEC noted that a possible GAVI investment in these would have a relatively small impact on mortality and low value for money compared with other possible investments, but recognized the localized epidemic potential of the disease. Although not a priority from a global impact perspective, the IEC felt that, given the relatively small size of the overall investment in a limited number of campaigns within an established policy environment, support for expanding yellow fever vaccination could be worthwhile considering, depending on the resource envelope. The Committee also felt that there could be a potential role for GAVI to play in shaping the market to overcome current capacity constraints.

Cholera

The IEC reviewed the "base case" vaccination strategy and agreed that this should be revised, as necessary, based on evolving evidence on appropriate age groups, frequency of campaigns and dosing. For example, a smaller target cohort (9 months to 5 years old) may be sufficient to protect the age group with the highest number of deaths and a 1-dose schedule may prove to provide sufficient protection. Updated study results should be factored into phase II analyses where available. The IEC validated the forecast in terms of country scope and subnational target groups for modeling purposes as an appropriate approximation of possible demand. The committee noted that herd immunity effects increase current estimates of impact. The IEC recognized the important role that oral vaccines could play to reduce (endemic and epidemic) cholera deaths in certain poor or fragile settings, while also noting that vaccination should not be a substitute for improvements in water and sanitation in the longer term. GAVI's role in supporting a stockpile for outbreak response could also be considered (though this falls outside the scope of the VIS). The Committee felt that supply constraints can be overcome and should not be considered a reason in and of itself for exclusion from Phase II analysis.

Measles

The IEC reviewed the modelled strategy for an incremental investment in measles (in addition to GAVI's existing support for measles second dose) focused on repeated cycles of three SIAs; the first campaign targeting children under 15 years old, followed by two SIAs in children under 5 years old. Pending an updated SAGE recommendation, the Committee posed questions regarding the need for targeting children under 15 years old, noting that deaths are highest in children under five, and requested an additional scenario of repeated SIAs in children under 5

years old (without the campaign in the larger age cohort). The committee supported the replacement (in the forecast) of measles campaigns with MR campaigns for those countries introducing rubella vaccines. Since MR introduction start with a catch-up campaign in children under 15 years old, the IEC asked to ensure that no additional under 15 year old campaigns are added to the described cycle of campaigns (one in children under 15 years old, two in children under 5) when overlaying with the rubella forecast within a country. The committee expressed concern that modelled impact represents a significant over-estimate for a number of reasons. First, the model used is deemed to over-estimate impact. In the absence of other (published) models, the Committee strongly suggested to do further 'plausibility checks' of impact estimates against, for example, measles burden data. Secondly, the Committee suggested modifying the 'counterfactual', by assuming a continuation of SIAs funded by other sources in the absence of GAVI support. This should result in a more realistic estimate of the incremental impact of potential GAVI investments. Thirdly, the IEC suggested reducing the country scope for GAVI's investment in additional campaigns based on risk and endemnicity. The Committee noted that any decision by the Board would need to articulate GAVI's desired role in measles in light of the overall programmatic objective (e.g. reducing deaths or contributing to elimination) as well as the broader funding environment.

Dengue

The IEC supported the "base case" vaccination strategy, focused on a catch-up campaign in an age cohort between two and 15 years old followed by routine vaccination of two year old children, but questioned the assumptions on routine coverage rates in this hard-to-reach age group. It also supported the limited country scope in the forecast given the lack of reliable burden data, particularly for Africa. There are significant uncertainties regarding the leading vaccine candidate, and efficacy results against one disease strain have been disappointing. However, regardless of coverage and efficacy assumptions, impact on mortality would be low. The committee noted that dengue cases may result in significant out-of-pocket expenses and as such would merit further economic analysis in future considerations. Overall, the committee felt that prospects for an appropriate vaccine as well as burden estimates are currently too uncertain. However, the epidemic potential and notable morbidity of the disease, with indications of burden in Asia and beyond, as well as the likely high community demand for a dengue vaccine, justify continued monitoring by GAVI of vaccine development in this disease area as the candidate vaccine comes closer to licensure.

Hepatitis A

The IEC supported a "base case" vaccination strategy focused on the routine immunization of 12 month olds with a single dose of Hepatitis A vaccine in countries that meet the WHO definition for intermediate endemnicity. This strategy is aligned with the recommendations in the 2012 WHO position paper. The IEC recognized that that Hepatitis A vaccine has relatively low potential for impact on mortality in GAVI-eligible countries. Due to this relatively low potential impact, the IEC did not advise that Hepatitis A would be a high priority for further evaluation in Phase II of the VIS process. The small country scope and limited time period between when a country's burden increases (due to the transition from high to medium endemnicity) and when the country is able to afford the vaccine also support this advice.

Hepatitis B

The IEC supported a "base case" vaccination strategy of a single dose vaccination at a healthcare institution within twenty-four hours of birth (per the WHO recommendation), but pointed out that an alternative scenario of vaccination outside of institutions (potentially using compact prefilled auto-disable devices and temporarily taking Hepatitis B vaccine out of the cold

chain) could also be considered. Two additional analyses were requested. First, additional analysis of data on the percentage of births that happen at institutions as well as recent trends was requested in order to check the coverage assumptions used in the demand forecast. Second, additional analysis of Hepatitis B coverage data since 2000 was requested to estimate what percentage of pregnant women in 2015-2030 will have been vaccinated. This in turn will provide a general sense of the degree to which the impact model is overestimating impact due to its utilization of 2012 prevalence data. Pending these updates to the analysis, the IEC noted the relatively high potential impact of Hepatitis B birth dose based on the current estimates. The IEC also recognized that the current cost of Hepatitis B vaccine is below the GAVI co-financing threshold, which calls into question what role GAVI would play in supporting this vaccine. If Hepatitis B birth dose is carried forward for deeper evaluation in Phase II, the IEC noted that country interest will be an important additional factor to take into account.

Hepatitis E

The IEC supported a "base case" vaccination strategy focused on the routine immunization of adolescent girls, given the high case fatality rate in pregnant women. However, the Committee recommended that the target population be 10 year old girls (to align with the target population for HPV) rather than 16 year old girls (the youngest age for which the vaccine is currently indicated). In general, the Committee felt that VIS assessments should take into consideration existing product profiles, but in this instance felt an exception would be appropriate given the high likelihood that a vaccine that was safe and effective in 16 year olds would also be safe and effective in 10 year olds. It was noted that limited disease burden data is available at the country level and more research is needed on Hepatitis E epidemiology and burden of disease. Based on the burden data available, the IEC advised that the country scope for the demand forecast be restricted to GAVI-eligible countries in Asia where the disease burden is the highest. However, given the currently available burden data and resulting impact estimates, the IEC did not deem hepatitis E to be a strong priority for further evaluation under the VIS process.

Influenza

The IEC supported a "base case" vaccination strategy focused on immunization of pregnant women at their first antenatal visit, which aligns with the 2012 WHO position paper recommendation. The IEC recognized the relatively high potential health impact of this strategy on maternal mortality as well as mortality in children under 6 months of age. The value of this vaccine in strengthening the antenatal contact point and continuing to build the platform for maternal immunization was also recognized. However, the IEC also noted two key challenges that will require further evaluation. First, there are policy and manufacturing challenges associated with strain recommendations for potentially year-round supply to GAVI-eligible countries. Second, there is low awareness of disease burden and therefore low demand at the country level, but Committee members felt that demand could be generated, especially in the target group of pregnant women.

Meningococcal ACWY

The IEC supported a "base case" vaccination strategy focused on routine immunization at 9 months with two doses of Meningococcal ACWY conjugate vaccine, replacing MenAfriVac in the meningitis belt. The IEC recommended that the country scope for the demand forecast be changed from all GAVI-eligible countries in Africa and Asia to GAVI-eligible countries in the meningitis belt only, given the significantly higher disease burden in these countries. While recognizing the disruptive potential of meningococcal meningitis outbreaks and long-term sequelae experienced by approximately 10-20% of survivors, the IEC noted the low potential incremental impact of protection against the C, W and Y serogroups on mortality and the high

relative cost of the vaccine. For future evaluations, the IEC noted that the potential evolution from a monovalent conjugate vaccine to a polyvalent conjugate vaccine should be reconsidered when a low cost polyvalent conjugate vaccine is closer to licensure.

Rabies

The IEC supported a "base case" vaccination strategy focused on intradermal administration of post-exposure prophylaxis (PEP), supplementing PEP support already provided by countries. One key challenge associated with this strategy is the risk of substitution of GAVI funding for current country funding of PEP. The IEC felt this was a significant risk, but one that could be managed by making GAVI funding contingent on country performance indicators. For example, IEC members discussed the possibility of GAVI support being contingent on country support for mass dog vaccination programs. A second key challenge discussed was the need to ensure supply in rural areas. Still, the IEC recognized that rabies is a pro-poor and cost-effective vaccine that can have a high impact on mortality relative to the other vaccines in the VIS scope. The IEC also recognized that while rabies is not a new vaccine, GAVI may consider whether it could have a catalytic role to play in expanding access, reducing cost through intradermal administration and promoting integrated rabies control programs.

Considerations for future investment decisions

- The IEC suggested the Board may want to ensure significant uncertainties linked to vaccines still under development are reflected. This can be achieved qualitatively or by discounting the benefits and costs of the investments.
- The IEC suggested that smaller overall investments with modest impact could be evaluated based on their catalytic potential.
- The IEC noted that while later impact should not necessarily be discounted over earlier impact, the timing of investments should be considered.
- The IEC noted that with an expanding menu of options, GAVI countries may benefit in future prioritization exercises from cost-effectiveness models that would combine several of the VIS evaluation criteria to provide an additional data point to inform decision-making.

C. Summary of key analysis outputs for vaccines under consideration (2015-2030)⁴

	U5 future deaths averted	Total future deaths averted	Total future cases averted	Total / GAVI procurement cost	Vaccine cost per death / case averted	Country adoption forecast	Total number of doses
Polio	N/A	N/A	N/A	\$680M / \$420M	N/A	56	720M
Malaria	440,000	440,000	75M	\$2.8B / \$2.2B	\$6,400 / \$37	34	800M
Rabies	36,000	210,000	210,000	\$75M / \$56M	\$350 / \$350	47	69M
Flu	170,000	200,000	5.8M	\$480M / \$330M	\$2400 / \$84	48	400M
Cholera	74,000	120,000	3.3M	\$1.0B / \$660M	\$8,600 / \$320	19	880M
Yellow fever	720	77,000	380,000	\$64M / \$64M	\$830 / \$170	9	67M
Dengue	700	4,600	2.7M	\$1.3B / \$1.3B	\$290,000 / \$490	7	610M
Meningitis	32,000	32,000	320,000	\$3.5B / \$2.7B	\$110,000 / \$11,000	26	620M
Measles	10,700	12,000	510,000	\$400M / \$300M	\$34,000 / \$790	51	540M
Hepatitis A	80	1100	320,000	\$43M / \$32M	\$40,000 / \$130	4	18M
Hepatitis B	0	110,000	1.5M	\$73M / \$25M	\$650 / \$50	36	210M
Hepatitis E	0	20,000	1.0M	\$350M / \$280M	\$18,000 / \$350	10	170M
VIS median ¹	5,000	32,000	660,000	\$440M / \$370M	\$9,000 / \$350	-	-

⁴ Estimates based on individual disease forecasts. In phase II, forecasts will be integrated, which will decrease cost and impact estimates for this time period.

D. Members of the Technical Consultation Group for the Vaccine Investment Strategy 2013

Name	Institution
Carsten Mantel	WHO
Meredith Shirey	UNICEF Supply Division
Robert Oelrichs*	World Bank
Orin Levine**	Bill & Melinda Gates Foundation
Anonh Xeuat	Ministry of Health, Lao DPR
Dafrossa Lyimo	Ministry of Health, Tanzania
Alfred da Silva	Agence de Médecine Préventive
Susan McKinney	United States Agency for International Development
Anders Molin	Swedish International Development Cooperation Agency
Anthony Scott	London School of Hygiene and Tropical Medicine
John Marshall	Independent
Bruce Gellin***	Independent
Aurelia Nguyen	GAVI Secretariat
Alan Brooks	GAVI Secretariat

* Represented by Tayyeb Masud at 11 March 2013 meeting

** Represented by John Yang at 30 January 2013 meeting and Damian Walker at 11 March 2013 meeting

*** Chair of 11 March 2013 meeting

The GAVI Secretariat project team for the Vaccine Investment Strategy consists of Alan Brooks, Santiago Cornejo, Eliane Furrer, Hope Johnson, Judith Kallenberg, Melissa Ko, Aurelia Nguyen and Laura Stormont.

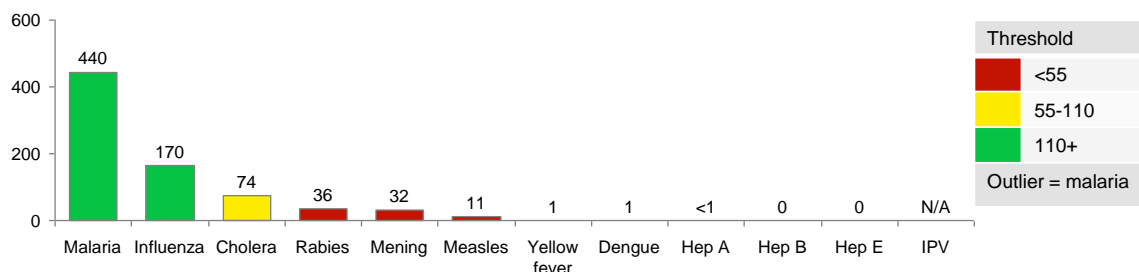
E. Members of the Independent Expert Committee for the Vaccine Investment Strategy 2013

Name	Institution	Title
Robert Black (CHAIR)	Bloomberg School of Public Health, Johns Hopkins University	Professor and Chairman, Department of International Health
Jane Achan	Uganda Paediatrics Association	President
Raj Bhan	University of Delhi, India	Professor
Fred Binka	University of Health and Allied Sciences, Ghana	Vice Chancellor
Kalipso Chalkidou	National Institute for Health and Care Excellence (NICE), UK	Director, NICE International
Melinda Moree	BIO Ventures for Global Health	Former CEO
Helen Rees	Wits Reproductive Health and HIV Institute, South Africa	Executive Director
Anne Schuchat	Centers for Disease Control and Prevention, USA	Director, National Center for Immunization and Respiratory Disease

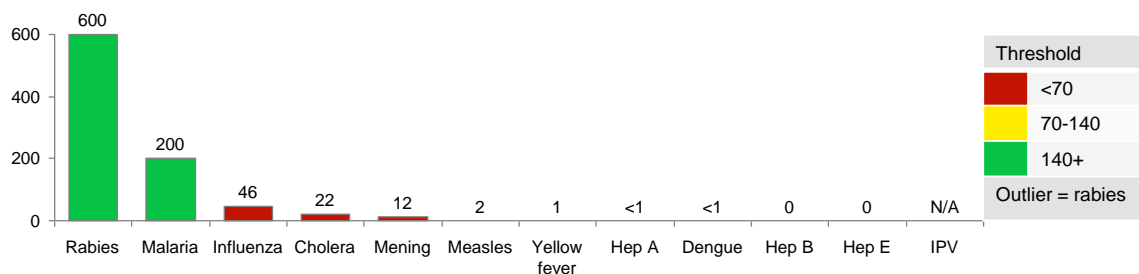
F. Summary of health impact outcomes by vaccine⁵

Under 5 deaths

1a. Under 5 future deaths averted, 2015-2030 ('000)

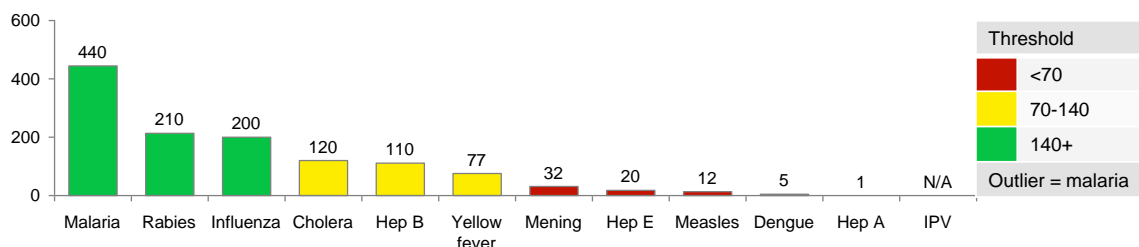


1b. Under 5 future deaths averted per 100K vaccinated, 2015-2020

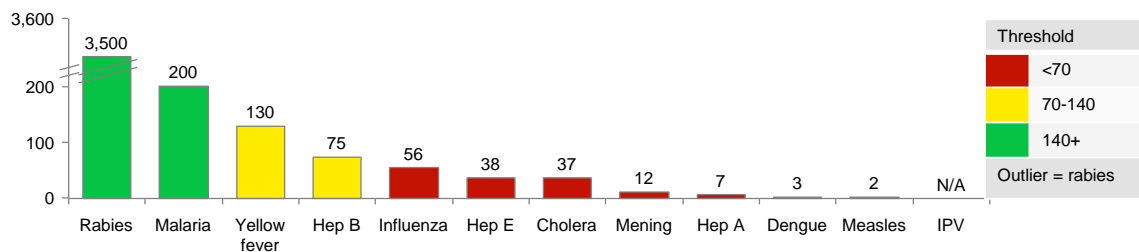


Total deaths

2a. Total future deaths averted, 2015-2030 ('000)



2b. Total future deaths averted per 100K vaccinated, 2015-2030



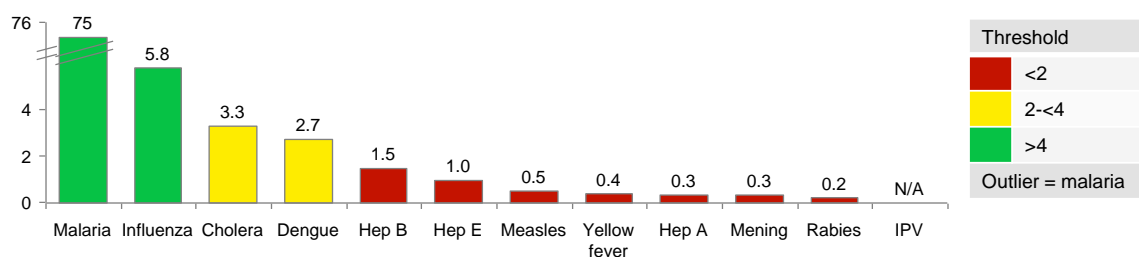
Comparison deaths averted per 100k vaccinated for current GAVI vaccines:

- Green: HPV, penta, rota, pneumo
- Yellow: JE, rubella
- Red: N. meningitidis serogroup A (routine)

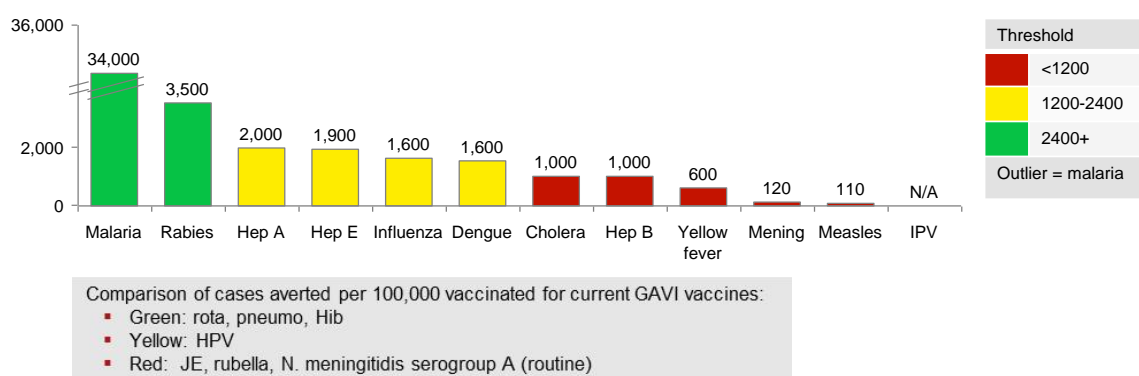
⁵ Estimates are based on currently modelled strategies and assumptions as summarised in Annex A

Cases

3a. Total future cases averted, 2015-2030 (Millions)



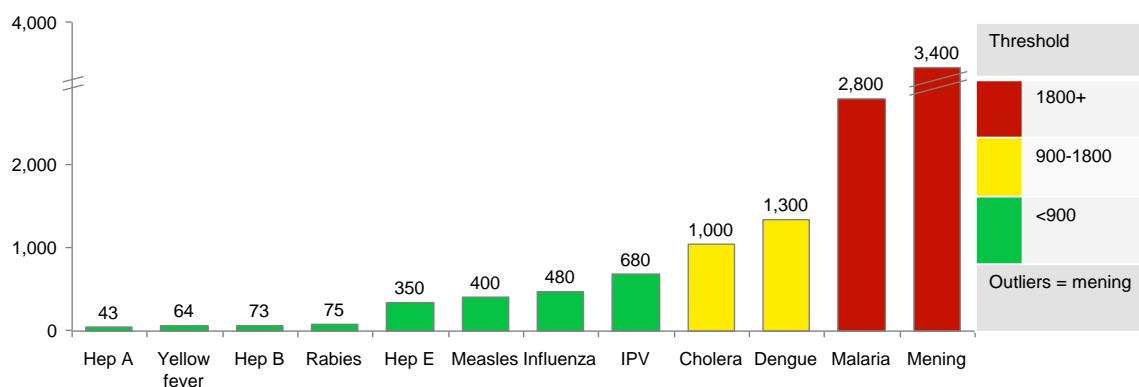
3b. Total future cases averted per 100K vaccinated, 2015-2030



G. Summary of cost and value for money outcomes by vaccine

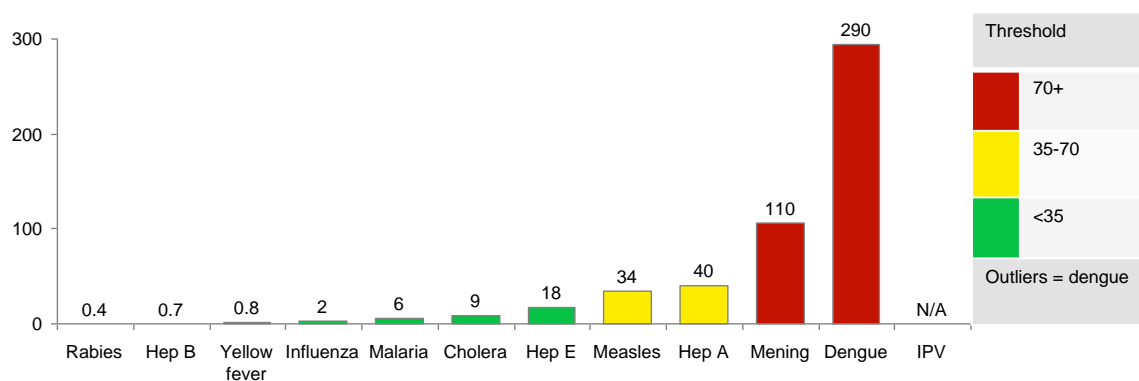
Cost

1. Total procurement cost⁶, 2015-2030 (USD, Millions)



Value for money

2. Cost per death averted, 2015-2030 (USD, '000)



⁶ Cost estimates reflect the cost of all forecasted vaccine procurement, including of vaccines financed by GAVI, co-financed by countries and financed by countries that have graduated following introduction with GAVI support.

H. Expert consultations

GAVI would like to thank individuals from the following organisations for their contributions to the VIS process.

- World Health Organization
- Bill & Melinda Gates Foundation
- UNICEF
- PATH
- Centers for Disease Control and Prevention
- International Vaccine Institute
- Malaria Vaccine Initiative
- Dengue Vaccine Initiative
- Swiss TPH
- National Institute of Cholera and Enteric Diseases
- International Centre for Diarrhoeal Disease Research, Bangladesh
- Agence de Médecine Préventive
- Global Alliance for Rabies Control
- Johns Hopkins University
- London School of Hygiene and Tropical Medicine
- University of California, Los Angeles
- University of Oxford
- Imperial College of Science, Technology, and Medicine
- Sanofi Pasteur
- GlaxoSmithKline
- Serum Institute of India
- Inovax
- Institut Pasteur