

SUBJECT: GAVI'S CONTINUED ROLE IN YELLOW FEVER CONTROL

Agenda item: 14

Category: For Decision

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1. Executive Summary

1.1 Rationale

- (a) The recent Yellow Fever (YF) outbreaks in Angola and DR Congo, and subsequent cross-border and intercontinental spread of the virus, underline the global public health threat that YF represents. YF virus is endemic in 47 African countries, 30 of which are Gavi-eligible, as well as 13 non-Gavi eligible countries in Central and Latin America. Moreover, factors facilitating YF virus transmission are evolving and thus the risk of YF outbreaks is increasing, particularly in urban environments. These factors include the widening distribution of the Aedes vector, increasing rates of urbanisation, population movements, ease of travel, climate change, increasing exposure of humans to infected mosquitoes and growing numbers of unimmunised individuals, the latter due in part to low levels of routine immunisation. The risk of outbreaks can be substantially reduced by increasing population immunity to >70%, which will be achieved through a wide age-range campaign and subsequent introduction into routine immunisation with high coverage.
- (b) Gavi has a long-standing commitment to YF control and since the Alliance's creation in 2000 has invested nearly US\$ 300 million, supporting the vaccination of over 200 million people in Africa. Gavi's investments have been aligned with WHO-recommended vaccination strategies and have supported the introduction of YF vaccine into routine immunisation programmes (17 countries to date), the implementation of wide-age range mass preventive vaccination campaigns in high-risk countries (14 countries) and access to the emergency vaccine stockpile to rapidly respond to confirmed YF outbreaks (16 countries)
- (c) Experiences in West Africa illustrate the effectiveness of this three-pronged strategy to prevent YF outbreaks when effectively implemented. Since 2006 when Gavi's support for mass preventive campaigns began, no YF outbreaks have been detected in West

African countries that have applied the recommended strategies. An extension of these proven strategies has however been hampered by systemic immunisation programme weaknesses, leading to low routine YF immunisation coverage and uptake, and by global vaccine supply constraints ensuing from production problems experienced by two of the four WHO pre-qualified manufacturers from 2013-2015.

- (d) Faced with an increasing risk of large urban YF outbreaks, WHO has revised its global long-term YF control strategy to “Eliminate Yellow Fever Epidemics”, (EYE). The development of this strategy coincides with an improved vaccine supply outlook. Close collaboration between the Gavi Secretariat, Alliance partners and vaccine manufacturers has resulted in investments in capacity and production improvements that will see supply capacity double from 72 million doses in 2015 to 140 million doses in 2020. Approximately 90 million more doses will be available through 2020 than was reflected in the financial forecast approved by the Board in December 2015, creating an opportunity to significantly scale up yellow fever control efforts.

1.2 Purpose

- (a) This report describes proposed changes to Gavi’s engagement in yellow fever, which the Programme and Policy Committee (PPC) recommended to the Board at its meeting on 25-26 October 2016.
- (b) The Audit and Finance Committee at its meeting on 21 October 2016 noted that it had reviewed the financial implications of this and other potential funding decisions that may be considered by the Board and concluded that these decisions could be approved by the Board in accordance with the Programme Funding Policy.

1.3 Salient features

- (a) The updated and revised WHO EYE strategy was discussed and endorsed by SAGE on 20 October 2016 and aims to protect at risk populations, prevent international spread, and rapidly contain outbreaks. The Gavi Secretariat has been engaged with WHO and other stakeholders in the development of the strategy and will continue to play a key role, notably in the proposed governance structure, as the strategy is further detailed and operationalised.
- (b) In line with the EYE strategy, Gavi’s approach to YF control will continue to focus on the three core vaccination strategies. The increased availability of supply will allow phased completion of mass preventive campaigns in three priority countries (Nigeria, Sudan and Ghana) which were previously delayed due to supply constraints as well as the introduction of routine YF vaccine in four countries (Uganda, Ethiopia, Sudan and South Sudan) on accelerated timelines. It will also enable an expansion of the emergency stockpile to ensure that 6 million doses of vaccine are available at all times.

- (c) As part of the EYE strategy, partners have agreed that new mechanisms will be necessary to strengthen governance, accountability and advocacy of YF control efforts at the global and country levels. Gavi will engage in these mechanisms as follows:
- i. The Secretariat will actively participate in the proposed steering committee and the relevant working groups for implementation of the EYE strategy. This will enable improved coordination, communication, decision making and planning for issues including market shaping, dose allocation and country prioritisation.
 - ii. Joint Appraisals and other review mechanisms will be used to identify reasons for low routine immunisation coverage and design and support activities to address these through Health System and Immunisation Strengthening (HSIS) grants and/or the Partners' Engagement Framework (PEF) and other immunisation system strengthening efforts.
 - iii. The Secretariat will actively engage with the International Coordinating Group (ICG) for yellow fever and partners to implement Gavi's new approach to stockpiles subject to that being approved by the Board. This will include joining the annual closed meeting of the ICG and requesting to being an observer to ICG decisions, as recommended by the PPC, to improve accountability, transparency and preparedness in outbreak response efforts.

2. Recommendations

The Gavi Alliance Programme and Policy Committee **recommended** to the Gavi Alliance Board that it:

- a) **Agree** that Gavi's support for Yellow Fever vaccine be based on the Eliminating Yellow Fever Epidemics Strategy developed by WHO (the "EYE Strategy").
- b) **Note** that due to increased supply availability, and the identified need to improve Yellow Fever vaccine coverage in endemic countries, to introduce forecasted expenditure on Yellow Fever vaccine support in Gavi eligible countries in the period 2017-2020 will increase by approximately up to US\$ 150 million.

Attachment

Appendix 1: Gavi's continued role in yellow fever control: Report to the PPC, 25-26 October 2016, Doc 09

SUBJECT:	Gavi's continued role in yellow fever control
Agenda item:	09
Category:	For Decision
Authored by:	Stephen Sosler, Patience Musanhu, Aaban Butt, Michael Clark and Jon Pearman

Section A: Overview

1. Purpose of this report

- 1.1 As requested by the PPC in May 2016, this report seeks endorsement of proposed intensification of Gavi's engagement in yellow fever in partial support of the World Health Organization's revised global Yellow Fever (YF) control strategy, pending endorsement by the Strategic Advisory Group of Experts on Immunisation (SAGE) on 26 October 2016.

Section B: Content

2. Gavi's engagement in YF control

- 2.1 Overall, Gavi has invested more than US\$ 300 million in support of YF control based on the following three vaccination strategies:
- (a) **Routine immunisation in high-risk countries:** In 2000, Gavi made its initial investment in YF to support the introduction of routine YF vaccine for all endemic Gavi countries. More than US\$ 122 million has been invested for YF routine immunisation, with 92 million children vaccinated in 17 African countries by 2015.
 - (b) **Emergency vaccine stockpile:** In 2002, Gavi commenced funding the global emergency vaccine stockpile for YF and by 2015 has disbursed US\$ 30 million in YF vaccine to countries to conduct vaccination campaigns to confirmed YF outbreaks.
 - (c) **Mass preventive vaccination campaigns:** Since 2006, first in support of the Yellow Fever Initiative and then through the Vaccine Investment Strategy, Gavi has invested over US\$ 97 million to support the implementation of wide-age range preventive vaccination campaigns in 14 countries. Overall, 99 million people have been vaccinated.
 - (d) An additional US\$ 51 million has been invested for operational costs for both reactive and preventive campaigns until 2015.

3. WHO's revised global strategy: Eliminate Yellow Fever Epidemics (EYE), 2016 - 2026

- 3.1 The recent YF epidemics in Angola and DR Congo (DRC) underline the global health threat that YF still poses and the particular risk of urban outbreaks in under-immunised populations, which can contribute to rapid human transmission with spread within and beyond national borders. They also highlight the changing disease epidemiology driven by factors such as urbanisation, large population movements, climate change, and increasing exposure of humans to infected mosquitoes in jungles and forests.
- 3.2 Faced with an increasing risk of large urban YF outbreaks, WHO has revised its global long-term YF control strategy. The revised comprehensive strategy, to "Eliminate Yellow Fever Epidemics", (EYE), aims to: protect at risk populations; prevent international spread; and rapidly contain outbreaks.
- 3.3 The Strategy maintains the existing three-pronged vaccination approach, namely combining high routine YF immunisation coverage with mass preventative vaccination activities in at-risk countries or populations as required, and timely vaccine response when cases arise through the global vaccine stockpile.
- 3.4 While there are many similarities between the revised EYE Strategy and earlier YF initiatives, there are also important strategic and programmatic differences including:
 - (a) A revised risk classification to guide preventive strategies in countries with a new three step methodology to: estimate crude risk based on empirical timing and intensity of YF virus transmission, modelled geographic transmission of potential and resulting disease burden; assess actual risk based on population immune/non-immune estimates; and prioritise the highest risk countries for mass preventive campaigns.
 - (b) Proposed catch-up vaccination for children born after previous mass vaccination campaigns but prior to the introduction of routine YF vaccine, depending on the availability of vaccine supply.
 - (c) Ensuring an emergency vaccine stockpile of 6 million doses is available at all times. This is a change from the previous approach of an annual stockpile that could and has been depleted during a year, requiring ad-hoc replenishment. The Strategy also revises previous plans calling for a reduction in the size of the stockpile to 2 million doses by 2020.
 - (d) Focusing more narrowly on reducing the risks of outbreaks, particularly urban outbreaks, reinforcing International Health Regulations (IHR) and global health security.
 - (e) Establishing a more robust governance structure, led by a steering committee of core partners, including Gavi, to lead the coordination, management and strategic direction of the programme. In addition,

technical working groups will be defined and report to the steering committee on a range of issues (e.g. vaccine market shaping, laboratory and surveillance capacity, vector control, etc.).

- 3.5 Developed within a constrained timeframe, the Strategy acknowledges that further consultation with countries and stakeholders is required to refine the assessment of risk and prioritisation of countries recommended for mass preventive vaccination campaigns (see Annex A). The strategy will be reviewed by the WHO's Strategic Advisory Group of Experts on Immunisation (SAGE) the week before the PPC. The Secretariat and WHO will provide additional detail on the EYE strategy and the SAGE discussion at the PPC meeting.

4. Evolving supply landscape

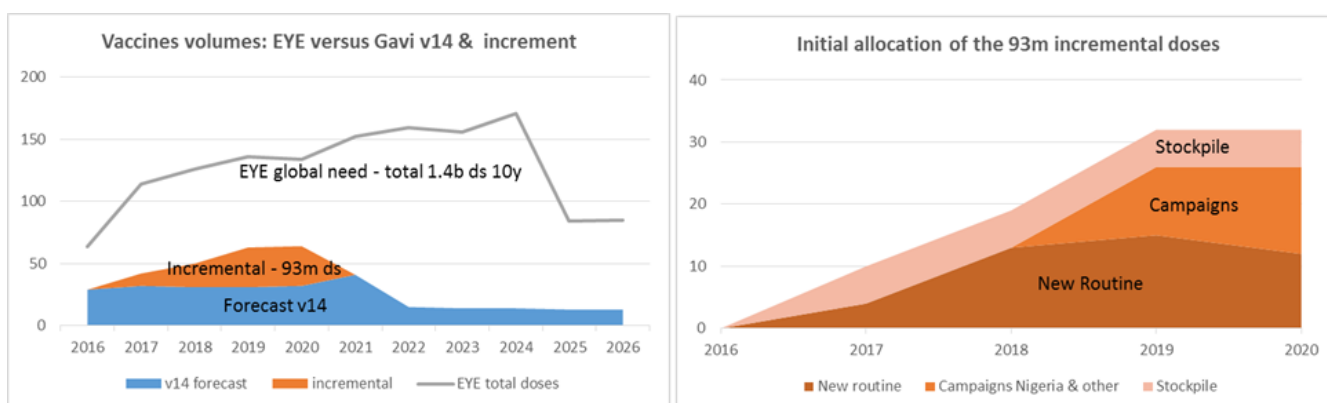
- 4.1 The EYE comes at a time of improving YF vaccine supply following several of years of insufficient global vaccine production that have impacted the implementation of forecasted and planned activities.¹
- 4.2 Available YF vaccine supply was 10 to 20% below demand during the period 2013-2015. Resolution of technical production issues at two of the four suppliers has resulted in the lifting of WHO prequalification suspensions. In addition, close collaboration between the Alliance and industry has resulted in investments in capacity and production improvements by all four suppliers². Together, these are expected to increase production capacity over the next 5 years with annual global production rising from 72m doses in 2015 to approximately 140m doses by 2020 (a 92% increase). This means that approximately 90 million more doses will be available through 2020 than was reflected in the financial forecast approved by the Board in December 2015.

5. Recommendation of Gavi's approach to support the implementation of the EYE strategy

- 5.1 The availability of additional supply provides an opportunity to intensify Gavi's support for yellow fever control efforts to meet country demand and contribute to implementing the recommendations of the EYE Strategy. Gavi proposes to use these doses to enhance its support for routine YF vaccination, mass preventive vaccination campaigns and the global emergency stockpile as follows:

¹ This includes delayed preventive campaigns in Nigeria and Sudan.

² Between the 4 suppliers: the following investments have been made during 2013 and 2016: a) construction of a new facility, b) Full refurbishment of three facilities c) Investment in additional fill/finish equipment d) Temporary use of alternate fill/finish capacity to meet surge demand. Further investments are expected to increase production from 2021 and confidence in supply reliability has increased.



(a) Support for routine YF vaccination: Gavi will strengthen its support in this area in two ways:

- I. Encourage introduction of routine YF vaccine: Four Gavi-eligible countries that are considered to be at high risk for YF have not introduced YF vaccine into their routine EPI schedules (Sudan, South Sudan, Uganda and Ethiopia)³. Gavi can assist in understanding the root causes for non-introduction associated with competing priorities and use non-financial levers to encourage countries to introduce. This will include requiring a commitment to routine introduction within 12 months as a condition of mass preventive campaign support, consistent with Gavi's revised measles and rubella strategy.
- II. Increase coverage of routine YF vaccine: YF coverage is strongly linked to the overall performance of national immunisation programmes but there are also vaccine-specific barriers that need to be better understood (e.g. wastage concerns due to vial size, multiple injections at the same visit). Coverage discrepancies often exist between measles first dose (MCV1) and YF. Understanding where and why these discrepancies occur and designing activities to ensure better convergence should be explicitly discussed during regular programme reviews and detailed during annual Joint Appraisals. Potential solutions can be financed through Gavi's health system and immunisation strengthening (HSIS) grants and / or the Partners' Engagement Framework (PEF). Countries with low RI coverage will be requested to submit plans on how to improve coverage during Joint Appraisals and renewal processes. Routine YF coverage can also be improved by harnessing immunisation strengthening activities for other similarly timed vaccinations, particularly measles and meningitis A.

(b) Mass preventive vaccination campaigns: Gavi supports the use of mass preventive vaccination campaigns as a proven-effective strategy to rapidly raise population immunity levels. Some activities planned in the highest risk countries, including Nigeria and Sudan, have not been

³ Sudan and Uganda have had lab-confirmed YF outbreaks, Sudan in 2012 and Uganda 2016. Ethiopia had confirmed cases in May – June 2013

undertaken due to vaccine supply constraints. These should be conducted as a matter of priority. Gavi will work with WHO and partners through the proposed governance structure to ensure that planning and sequencing of campaigns is based on agreed criteria that takes into account risks, benefits and trade-offs related to an alternative mix of strategies. While EYE proposes a sequence for mass preventive campaigns, more engagement with countries and partners is required to ensure national commitments are in line with supply capacity.

- (c) Emergency vaccine stockpile: Gavi will provide additional financing to maintain a standing stockpile of 6 million doses. In addition, the Secretariat will work with the International Coordinating Group (ICG) and partners to apply the new approach to Gavi's investment in stockpiles being proposed to the PPC (see Doc 08).

5.2 In addition, Gavi will continue to apply its comparative advantage and expertise to affect a healthier YF vaccine market. The Alliance has already worked with manufacturers to increase supply capacity by sharing demand forecasts, providing technical support to two manufacturers, and facilitating and actively monitoring each manufacturer's progress. Overall, confidence in supply reliability has increased due to improved processes and upgraded equipment by all manufacturers. However, the market will not be able to meet demand requirements if countries fully implement the vaccination activities recommended by the EYE strategy. To address this, Gavi will continue to work with manufacturers to scale-up capacity for additional supply increases from 2021 as well as with countries to balance potential demand. Engagement with manufacturers will also be required to consider alternative production schedules to ensure year-round availability and production of vaccine. Fundamental to this work will be determining the optimum size of the revolving stockpile vis-à-vis trade-offs with implementation of mass preventive campaigns and the potential risk of an eventual Asian YF outbreak.

5.3 As proposed in the EYE Strategy, Gavi will participate as a core member of the Steering Committee as well as the technical sub-groups as required. These fora will provide an opportunity to discuss in greater detail areas of the EYE Strategy that require more explanation and consensus as the plan is implemented. For example:

- (a) More explicit presentation and discussion of categorization of country risk that leads to the recommendation of mass preventive campaigns and the sequencing of these activities, balancing the risks and benefits of different scenarios.
- (b) Determination of the optimum size of the emergency stockpile. For example, should the stockpile be scaled differently over the next ten years with a larger stockpile at the beginning and gradually declining as population immunity levels increase?
- (c) Surveillance for yellow fever is and will remain a critical public health activity for the early detection of sylvatic or urban cases and optimal

vaccination response. It is necessary to assess the feasibility and affordability of increased surveillance capacity, including the introduction of point of care tests and other rapid diagnostics. Determining the engagement of different stakeholders and donors, including Gavi, at the global, regional and country levels will require further discussions.

Section B: Recommendations

5.4 The Gavi Alliance Programme and Policy Committee is requested to recommend to the Gavi Alliance Board that it:

- (a) **Agree**, subject to SAGE endorsement of the EYE Strategy, Gavi's support for Yellow Fever vaccine be based on the Eliminating Yellow Fever Epidemics Strategy developed by WHO (the "EYE Strategy").
- (b) **Note** that due to increased supply availability, forecasted expenditure on Yellow Fever vaccine support in Gavi eligible countries in the period 2017-20 will increase by approximately up to US\$ 150 million.

Section C: Risk implication and mitigation and Financial implications

6. Risks and mitigation

- 6.1 Lack of political will and commitment for inclusion of YF vaccine in the routine EPI can remain a barrier to achieving optimum coverage. National, regional and global advocacy and engagement with WHO and Alliance partners are critical to ensure the implementation of the prevention strategies recommended by the EYE Strategy. At the ministerial level, formal inter-country dialogues are required to ensure countries commit to disease control activities and IHR.
- 6.2 There is a risk that countries may continue to focus on preventive campaigns instead of routine immunisation as their primary disease control strategy. Gavi has not received applications for routine immunisation since 2008. The Alliance will need to engage closely with Ministries of Health to develop plans that prioritise routine immunisation and can leverage country applications for mass preventive campaigns by including requirements for routine YF vaccine inclusion and regular performance review.
- 6.3 There is a risk that supply capacity will be lower than forecasted (e.g. due to prolonged loss of production by one of the major manufacturers or delays in manufacturers' scale-up plans). The Alliance will continue to engage closely with manufacturers to support and monitor progress in scaling up supply capacity and also reprioritise key activities in line with supply capacity.
- 6.4 There is also a risk of vaccine supply over-capacity in the longer term as new capacity comes on-stream from 2022. Demand is expected to fall substantially from 2024 as the intensity of mass preventive campaigns is reduced, on the assumption there is no expansion of YF to other countries

including possible outbreaks outside the Africa region. For this reason, Gavi is monitoring but not actively encouraging the entrance of new manufacturers and providing transparent demand forecasts to manufacturers.

- 6.5 Risks related to demand may occur in two directions. The draft demand forecast may be overstated if countries do not rapidly increase yellow fever related vaccination efforts in line with the EYE strategy. This could undermine manufacturer confidence and affect their efforts to increase capacity. This risk must be mitigated by collaborative work between interested parties including manufacturers and countries to challenge and validate the demand forecasts to be complemented by efforts to encourage countries to prioritize YF control efforts. Global yellow fever plans and targets will be developed, monitored and discussed at national, regional or global platforms to strengthen the implementation of the program. Equally, demand could be higher than forecast if additional major outbreaks occur requiring large emergency response campaigns. In such cases, manufacturers have some surge capacity and an emergency plan would be discussed with manufacturers to meet levels of emergency demand, including the potential to temporarily divert (for 3 to 6 months) supply from preventive campaigns to meet the needs of outbreaks. Should more dramatic outbreaks occur, the use of fractionated doses may be considered.
- 6.6 The decrease of polio resources associated with polio transition may have an important impact on the field-level detection, biologic sample collection and reporting of vaccine preventable diseases (VPD) currently supported by GPEI funded staff, with negative consequences of timely immunization response activities. Gavi is a member of the Polio Transition Management Group and is working with a broad range of partners to develop national Polio Transition Plans and ensure relevant information is available during Gavi funding and support discussions (i.e. HSIS and PEF).

7. Financial implications

- 7.1 The revised strategy being proposed would add approximately US\$ 150 million to the forecasted expenditure presented to the December 2015 Board for the period 2016-2020. This includes approximately 90 million yellow fever vaccine doses, associated operational costs for campaigns and vaccine implementation grants for routine immunisation. This expenditure is incremental to the US\$ 278 million YF vaccine budget allocation presented to the Board as part of the financial forecast in December 2015 reflecting the availability of additional supply.
- 7.2 Since, there has not been a detailed country-level forecasting exercise to date, implementation plans and sequencing will need to be validated with countries, which could lead to further refinements in the forecast.

Appendix: Implications

8. Impact on countries

- 8.1 Gavi's comprehensive support for YF will continue to provide countries with predictable financing for vaccine procurement and health systems strengthening, as well as reinforce country ownership. Improved coverage of both routine immunisation and preventive campaigns will reduce the likelihood of YF outbreaks.
- 8.2 Countries will need to prioritise YF control efforts, understand reasons for poor coverage and develop strategies to ensure timely and effective delivery of yellow fever vaccines. This will require innovative strategies and careful monitoring and evaluation of implementation.
- 8.3 Historically, YF virus circulation has been predominately a Western African occurrence. Recently, however, outbreaks have occurred in East and Central Africa. Ensuring regional commitments and targets for improving YF vaccine uptake will require public policy and advocacy. The learnings from polio have shown the need for regional policies to bolster the necessary political support at national and regional level.

9. Impact on implementing partners

- 9.1 Gavi and its technical partners will need to engage with countries and provide strengthened technical assistance. The development and implementation of a YF long term strategy requires the coordination of a number of partners, including UNICEF SD, PAHO and countries as well as a transparent and effective mechanism for decision making about strategic tactical and operational issues. This will entail stronger systems for liaison and coordination around YF activities, including to manage YF vaccine supply and demand in a more integrated way.
- 9.2 Monitoring and evaluation framework developed by alliance partners with lead from WHO will also strengthen the implementation of the EYE strategy. After the PPC meeting it is important to facilitate a broader discussion and understanding, including with countries and have consensus on options for classification of risk, the mix of preventive strategies, and the prioritization of countries and subnational areas. This would address the issue of need a clear rationale for the selection of proposed options. Discussions are ongoing on implementing new coordination mechanisms.

10. Impact on Secretariat

- 10.1 Through the proposed governance structure, the expectations for improved programme monitoring and management are increased and will require increased engagement of the Secretariat. The intensity of engagement will vary by the component of the strategy but will monitoring vaccine demand, supporting country vaccine applications (preventive campaigns as well as RI), stockpile forecasting, procurement and market shaping.

11. Consultation

- 11.1 In preparing the EYE strategy, the World Health Organisation has engaged and coordinated with multiple stakeholders. An ad hoc advisory panel made up of YF experts received early drafts of the strategy; a WHO Technical Team made up of headquarters and regional staff managed the development of key work streams; core partners, including UNICEF, SAGE, Gavi and the Bill & Melinda Gates Foundation were consulted, as well as technical specialists. See Annex B with summary. Finally, a consultation meeting with more than 50 participants from different stakeholder groups was held in Geneva on 12 September 2016, where participants provided feedback on the strategy and technical inputs through working groups.
- 11.2 The Gavi Secretariat engaged with WHO throughout the process to provide feedback on the EYE strategy and to support WHO with specific inputs in the area of supply and market shaping.

12. Gender implications

- 12.1 Emerging evidence including from annual joint progress reports suggest that men and youths are frequently not turning up for preventative campaigns and strategies that promote health seeking behaviour should be employed as part of the preparedness plans.

Annexes (available on myGavi)

Annex A: Eliminate Yellow Fever Epidemic (EYE), document submitted to SAGE
26 Sept 2016

Annex B: Yellow Fever consultation summary

Annex C: Supply and Market dynamics

Annex D: Gavi Yellow Fever decisions