A WHO REPORT OF THE
Eliminate Yellow Fever Epidemics (EYE)
Strategy Annual Partners’ Meeting
2018

Dakar, Senegal
11–13 September 2018
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Acronyms

AFRO  WHO Regional Office for Africa
CDC   The Centers for Disease Control and Prevention (United States)
DRC   Democratic Republic of the Congo
ELISA Enzyme-linked immunosorbent assay
EYE   End Yellow Fever Epidemics
FIND  Foundation for Innovative New Diagnostics
Gavi  Gavi, the Vaccine Alliance
ICG   International Coordinating Group on Vaccine Provision
IFRC  International Federation of Red Cross and Red Crescent Societies
IHM   Infectious Hazards Management
LG    Leadership Group
MCV   Measles-containing-vaccine
MMR   Measles, mumps and rubella vaccine
PAHO  Pan American Health Organization
PCR   Polymerase chain reaction
PMG   Programme Management Group
UNICEF United Nations Children’s Fund
UNICEF SD United Nations Children’s Fund Supply Division
WHO   World Health Organization
WHO HQ World Health Organization Headquarters
YF    Yellow fever
The comprehensive global strategy to Eliminate Yellow Fever Epidemics (EYE) was developed by WHO, UNICEF, Gavi the vaccine alliance, and more than fifty partners to build a global coalition that will tackle the increased risk of yellow fever (YF) epidemics in a coordinated manner by 2026.

The annual EYE Strategy Partners Meeting was held on the 11–13 September in Dakar, Senegal, and hosted by UNICEF West and Central Africa Regional Office (WCARO). More than 70 participants, including partners, country representatives, vaccine manufacturers, donors, and experts came together to discuss the EYE Strategy achievements to date, and the main challenges that are anticipated going forward.

The main objectives of the meeting were:

- To review and discuss the EYE Strategy future plans and the way forward,
- To strengthen partners', particularly country partners', engagement,
- To discuss key issues relating to the Strategy's implementation.

The meeting opened with a summary of the Strategy's progress to date and situational updates from the WHO Regional Office for Africa (AFRO) and Pan American Health Organization (PAHO). This was followed by presentations on emerging research issues in YF control and updates from by the Strategy's working groups, including the new Immunization Operational Guidance working group. The EYE Secretariat also presented its work on the development of the EYE Country Guidance Toolkit, a resource for country-level partners with targeted and relevant advice on scaled-up approaches to rolling out YF control activities from epidemic investigation to immunization. The second day comprised of presentations from individual countries, and overview of vaccine supply and demand, and presentations from vaccine manufacturers. The third and final day included expert panel discussions and the presentation of proposed work plans by the working groups. The meeting ended with a summary and outline of the Strategy's next steps, followed by a guided tour of the Pasteur Institute in Dakar—the YF reference laboratory for the African Region.
The Strategy is currently on track to meet its objectives, and a number of achievements were highlighted. The EYE Governance Framework is operational with increasing interactions and engagement from representatives in the Programme Management Group, Leadership Group, and working groups. The new Immunization Operational Guidance Working Group was also established and the role of the Supply and Demand Working Group was expanded to improve coordination between vaccine supply and demand. Delegates also noted the significant progress that has been made towards the target of establishing three regional YF reference laboratories in the African Region. There has also been an increase in global vaccine supplies as a result of combined efforts by partners and strong engagement from vaccine manufacturers. The need to improve readiness in urban areas to protect populations was also highlighted, particularly as outbreaks in recent years have been unpredictable and the factors driving YF risk have changed. It was also noted that although the coverage gap between YF and other vaccine-preventable diseases such as measles is closing, challenges remain in terms of improving the performance of routine immunization for YF. Finally, improved information on YF risk and vaccine coverage is needed to inform campaign prioritization, identify populations most at risk and improve the visibility of vaccine needs.

Delegates provided their valuable input on how to move EYE forward in terms of governance, planning and implementation. Important technical priorities were identified, including effective prioritization of resources at a global level through assessment of YF risk, strengthening implementation of immunization (particularly routine immunization), and enhancing surveillance and laboratory capacity. All partners agreed on the key role of country commitment and ownership in unlocking the potential of the Strategy by implementing mass preventive immunization campaigns and scaling up routine immunization with the support of the EYE Programme Management Group (PMG) comprising representatives from WHO, Gavi and UNICEF. Other achievements in terms of the Strategy’s governance include the establishment of the new Immunization Operational Guidance Working Group and the expansion of the Supply and Demand Working Group’s role.

The meeting provided a forum for open discussion not only on the Strategy’s successes to date and examples of best practice, but also challenges and constraints. The EYE partners and working groups closed the meeting with agreement on their work plans going forward and reaffirmed their commitment to achieving the Strategy’s objectives. Delegates identified action points to move forward with the Strategy’s implementation in the coming years.
1. Background

Yellow fever (YF) is a flavivirus primarily transmitted by Aedes and Haemogogus mosquito species. It is difficult to diagnose due to the often non-specific presentation of clinical symptoms, and case identification is often complicated by the co-circulation of other flaviviruses and cross-reactivity when using currently available diagnostic tools. Effective case-based surveillance, laboratory confirmation and strong investigation are critical for establishing the presence of an outbreak. Forty countries across Africa and Central and South America are classified as high-risk or with high-risk areas for the disease.

Humans are not the sole reservoir of the virus, and this means that YF can never be fully eradicated. However, the risk of YF outbreaks can effectively be controlled through vaccination of all at-risk populations. A single dose of vaccine is effective in more than 95% of recipients, with protective antibodies appearing 7–10 days after immunization.

The previous YF control strategy, the Yellow Fever Initiative was established in 2006 as a collaborative initiative between WHO and the United Nations Children's Fund (UNICEF) with the support of Gavi, the Vaccine Alliance. It targeted endemic countries in Africa and supported introduction of YF vaccine into routine childhood immunization programmes and preventive mass vaccination campaigns. The initiative resulted in a steady reduction in the yearly number of YF outbreaks. By 2015 no outbreaks were reported in the African Region. This situation changed in 2016, however, when two major urban outbreaks in Angola and the Democratic Republic of the Congo (DRC) (neither of which were classified as high-risk countries) with subsequent international spread to China, called for the development of a new global strategy to prevent and control YF.

In response, a coalition of partners working to stop yellow fever outbreaks met in Geneva on 12 September 2016 to develop a new strategy: Eliminating Yellow Fever Epidemics (EYE). This comprehensive global strategy was developed by WHO and partners to build a global partnership to tackle by 2026 the increased risk of yellow fever epidemics in a coordinated manner.

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The EYE has three Strategic Objectives:

1. **Protect at-risk populations**
   - Preventive mass vaccination campaigns
   - Vaccinate every child
   - Risk analysis to allocate resources

2. **Prevent the international spread of Yellow Fever**
   - Protect high-risk workers
   - Apply the international health regulations
   - Build resilient urban centres

3. **Contain outbreaks rapidly**
   - Strengthen surveillance and laboratory capacity
   - Ensure availability of emergency vaccine stockpiles
   - Immediate outbreak response

The first annual EYE Strategy Partners’ Meeting was held on 9–10 May 2017 and resulted in agreement on the next steps to carry the Strategy forward including the implementation of a new governance structure and the need to tackle technical priorities such as global risk evaluation. At its close, stakeholders agreed on four priority areas to be addressed over the following 12 months:

- Global prioritization of a matrix for vaccine allocation and implementation;
- Sustaining improvements in the vaccine supply situation;
- Increasing capacity to diagnose YF quickly and accurately; and
- Improving communication and engagement among partners.

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1.1. The EYE Strategy and its implementation to date

Building on the endorsement of the strategy by African Ministers of Health at the 67th WHO regional committee in September 2017, the EYE regional kick-off meeting for Africa was held in Abuja, Nigeria, on 10–12 April 2018. There, Dr. Tedros Adhanom Ghebreyesus, WHO Director-General, called on countries and other partners to reinforce their engagement to eliminate YF epidemics by 2026, and 11 countries in the African Region committed to national work plans for the Strategy’s accelerated implementation. The meeting was praised for bold declaration of intent and gave EYE partners the opportunity to share perspectives and affirm their long-term commitment to the Strategy. It also highlighted the need for strong engagement by countries to ensure success, robust communication strategies alongside mass vaccination campaigns targeted at the most vulnerable.

Achievements since the first annual Partners’ Meeting include the implementation of the EYE’s Governance Framework and the Strategy’s Leadership via the Programme Management and technical working groups’ whose terms of reference have now been defined. The groups are now working side by side to drive forward the Strategy’s implementation in both the African and PAHO Regions. There has also been an improvement in global vaccine supply, both in terms of quantity and reliability, as a result of improved market shaping and engagement with manufacturers. This underpinned by strong partnership with Gavi and vaccine manufacturers, in addition to increasing commitment and engagement from individual countries. Planning for preventive mass vaccination campaigns in Nigeria, Ghana and Sudan is already underway. Together, these campaigns are expected to reach over 35 million people by the end of 2018.

The Abuja meeting also emphasized the importance of expanding routine immunization, and the need to strengthen surveillance and laboratory diagnostic capacity in all high-risk countries. As of 2018 these remain major priorities for the strategy going forward.

Currently, the main priorities for the Strategy are:

• To implement preventive mass campaigns in at-risk countries to raise their populations’ level of immunity and control the heightened risk of outbreaks;

• To expand routine immunization, increase vaccination coverage to maintain the gains achieved by mass campaigns, and provide sustainable protection for populations most at risk; and

• To improve laboratory capacity to enable reliable, rapid and accurate confirmation of YF cases to trigger action—whether preventive or reactive.
1.2. EYE Strategy Partners’ Meeting, 2018

The Eliminate Yellow Fever Epidemics (EYE) Strategy Partners’ Meeting was held from 11–13 September 2018 at the King Fahd Palace Hotel in Dakar, Senegal. It was hosted by the UNICEF West and Central Africa Regional office (WCARO), and organized by WHO, Gavi and UNICEF with the support of the Senegalese Ministry of Health. The proceedings were guided by Dr Sylvie Briand, Director of the Infectious Hazards Management (IHM) Department at WHO, who opened the meeting and set its agenda.

Over 70 delegates participated, including representatives of the World Health Organization (WHO) headquarters (HQ), the WHO Regional Office for Africa (AFRO), the Pan American Health Organization (PAHO), United Nations Children’s Fund (UNICEF) West and Central Africa Regional Office, Gavi, the United States Centers for Disease Control and Prevention (CDC) and the International Federation of Red Cross and Red Crescent Societies (IFRC) and the Foundation for Innovative New Diagnostics (FIND). WHO and UNICEF country offices were also represented in addition to ministries of health from individual countries—including Nigeria, the DRC and Sudan. Representatives of vaccine manufacturers and academic partners were also in attendance.

The venue for the meeting was especially appropriate. Senegal is an example of a country at the forefront of YF control and an example of best practice that has the potential to be replicated throughout the African Region. The country is taking the lead not only in increasing immunization coverage but is also home to the YF reference laboratory for the African Region—the Pasteur Institute in Dakar. The meeting placed the emphasis on Africa as several countries in the Region are set to begin implementation of mass vaccination campaigns over the coming years. It provided a platform for country partners in the Region to give their inputs on the Strategy’s implementation and affirm their commitment to its realization. It also presented an opportunity for fostering collaborations and sharing experiences from both across the Region and between participants from Africa and the Americas.

The EYE Strategy Partners’ Meeting was held back-to-back with a meeting on the development of the EYE proposal for lab capacity and network strengthening in Africa, which took place on 14 September.
The objectives of the EYE Strategy Partners’ Meeting were:

- To review and discuss among global, regional and country EYE partners, key issues related to the implementation of the EYE Strategy;

- To review and discuss future plans for the EYE Strategy and the way forward;

- To strengthen partners’, in particular priority countries’, engagement; and

- To foster a healthy YF vaccine supply situation through improved demand forecasting and understanding of the YF vaccine manufacturers production capacity and viewpoints.

The first day of the meeting kicked off with an introduction on the meeting’s objectives and presentations outlining the latest regional perspectives on the current YF situation in the Americas and Africa. Stakeholders were then briefed on the Strategy’s progress to date and the latest research findings on combined vaccination campaigns. This was followed by presentations on emerging research issues in YF control including fractional dosing, and updates from the Risk Analysis, Laboratory, Vaccine Supply and Demand, and the new Immunization Operational Guidance working groups.

The second day included country updates from Senegal and Colombia, two countries which have led successful approaches to YF control in the recent past, and highpriority countries such as DRC, Ethiopia and Sudan where mass preventive and routine immunization will soon be rolled out with the support of the Strategy. This was followed by an extended session on vaccine supply and demand in the afternoon which outlined the YF vaccine supply outlook for 2017–2020. Vaccine manufacturers then presented their supply updates and plans for future production. The day finished with a manufacturer and expert roundtable session. Delegates were updated on new research perspectives on the evolution of the global risk of YF and possible mechanisms for risk reduction. The EYE Secretariat presented its work on the development of the EYE Country Guidance Toolkit—a resource aimed at country-level partners to provide practical guidance on accelerating the Strategy’s implementation. Feedback and guidance was sought from stakeholders to guide its development and ensure that it meets their specific needs ahead of its finalization.
The third and final day provided a forum for open discussion towards planning the roadmap for the Strategy’s implementation going forward and a recap of the previous days. The day was rounded off with a field visit to the Pasteur Institute in Dakar which featured an overview and guided tour of the laboratory facilities.

The three days of discussions brought together a critical mass of partners from across the globe with different expertise and a range of perspectives. All partners and donors expressed their deep appreciation and satisfaction at the end of the meeting and felt confident in moving forward with the Strategy’s near and long-term goals.

Figure 1. EYE in numbers

<table>
<thead>
<tr>
<th>Number</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 51M people</td>
<td>Protected through Routine Immunization programmes in Africa</td>
</tr>
<tr>
<td>&gt; 47M people</td>
<td>Protected through Preventive mass campaigns in Africa</td>
</tr>
<tr>
<td>&gt; 8.5M people</td>
<td>Protected through Reactive vaccination campaigns in Africa</td>
</tr>
<tr>
<td>~ 40</td>
<td>Calls of the Programme Management Group (PMG)</td>
</tr>
<tr>
<td>9</td>
<td>ICG requests reviewed</td>
</tr>
<tr>
<td>4</td>
<td>Gavi applications received for RI or mass campaigns</td>
</tr>
</tbody>
</table>
2. Global & regional epidemiological summaries & updates

From 2004 to 2015 the number of YF outbreaks per year in Africa had fallen from eight to zero; in part due to gains from the preventive mass vaccination campaigns carried out by the extensive Yellow Fever Initiative (YFI) between 2006 and 2014 in the highest-risk countries in West Africa. Countries such as Nigeria in West Africa, and others in Central and Eastern Africa, did not benefit from these mass campaigns and levels of population immunity remain too low to prevent epidemic amplification.

The risk of YF outbreaks has changed and their occurrence remains unpredictable. From 2006–2016, 80% of African YF events had occurred in areas where there were previously none. The large YF outbreaks in Angola, Brazil and the DRC which brought the virus to the doorstep of large urban centres where both natural immunity and vaccination coverage are low, were unexpected and occurred in areas not previously considered high-risk. Due to this uncertainty, outbreak response will remain a key element of the Strategy until population-level immunity has been increased as a result of mass and routine vaccination. Despite sustained progress in preventive mass vaccination at the country level, strengthening routine immunization remains crucial to securing the Strategy’s long-term success and sustainability.

The epidemiological characteristics of yellow fever differ between Africa and the Americas, and in both regions, there has been a shift in risk patterns. Risk has been amplified by environmental changes, evolution in land use patterns, and increasing intensity of human economic activity. Population movements not only risk accelerating the spread of YF, but also influencing levels of vaccines coverage at the local level as unvaccinated people move into endemic areas.

Yellow fever outbreaks occurred in both AFRO and PAHO countries in 2018, and Brazil, Nigeria and the Republic of the Congo were most affected. During the 2018 epidemic season the latter two countries made four vaccine requests to the International Coordinating Group (ICG) on Vaccine Provision, which oversees a continuously replenished revolving emergency stockpile of 6 million doses of yellow fever vaccine with the support of Gavi.
2.1 PAHO Region: Situation summary of yellow fever in the Americas

Thirteen countries in the Americas have endemic areas for YF. Environmental drivers of YF transmission in the region include deforestation and encroachment of humans on non-human primate habitats. Although urban YF outbreaks have occurred in the past, more recently YF has only been detected in sylvatic vectors (Haemogogus and Sabethes species) and transmission has only occurred in rural and peri-urban areas. Recently, attention has been paid to the emergence of ‘sylvatic corridors’, or forested areas which extend into peri-urban settings and facilitate epizootic spread occurring in waves which are believed to be linked to migrations of non-human primates. Further evidence on competency Aedes vectors (implicated in urban spread) for the YF virus is also needed to fully characterize YF risk in the region. A major challenge for YF surveillance is its co-circulation with other flaviviruses (such as Zika virus) which can hamper confirmation of cases.

Brazil became the focus of YF control efforts in the region in 2016 when the country experienced significant peri-urban transmission which threatened the potential re-emergence of YF in urban areas, previously not considered at risk, for the first time since 1942. Although the number of new cases per month has decreased since 2016, there were a total of 1,266 confirmed YF cases and 415 fatalities in Brazil from July 2017 to May 2018. Surveillance work has been targeted at identifying sylvatic corridors and confirming epizootic (non-human primate) cases, which totalled 656 from July 2017 to March 2018. The country has made significant efforts to address low vaccination coverage in urban areas. In January 2018 the country launched a mass vaccination campaign targeting 22.6 million people in São Paulo, Rio de Janeiro and Bahia states. Out of this total, 17.2 million people will receive fractional doses and the remainder will receive the full dose (children aged 9 to 24 months, pregnant women, international travelers and people with special clinical conditions). Brazil has expanded vaccination recommendation to the whole country and it is expected a total of 70 million people will have been vaccinated by the end of the year. Routine immunization is expected to be expanded across the entire country by 2019. Efforts are also being made to improve record systems to track individuals’ vaccination status. Challenges include reaching specific target groups, health system capacity to distribute vaccines, and acceptance of fractional dosing among public and medical professionals.

After a major outbreak in 2003–2004, Colombia has intensified YF control efforts. The country has made significant progress in expanding surveillance and laboratory capacity.
Colombia now boasts a network of local laboratories at the departmental level which send samples to the national laboratory in Bogotá. Progress has also been made over the last three years towards improving routine immunization coverage in infants. Challenges remain, however, including the co-circulation of other arboviruses, population movements, the presence of vulnerable groups and the need for faster case confirmation. Several YF cases were confirmed in the country during 2018.

Sporadic cases were also reported in other endemic countries in the Region during 2017, including the Plurinational State of Bolivia, Ecuador, and Peru. Sporadic cases among unvaccinated travellers were also detected in French Guiana and Suriname.

2.2 AFRO Region: Situation summary of yellow fever in Africa

Thirty-five countries, home to around 500 million people, are considered to be at some level of risk for YF outbreaks. Of these, 27 are considered to be at high risk of YF by EYE. Transmission occurs both via the sylvatic cycle, and the urban cycle in which Aedes aegypti vectors transmit YF directly between humans. YF risk in recent years has been driven by population movements (particularly that of mobile workers involved in resource extraction), in addition to population growth, deforestation and urbanization. Although previous mass vaccination campaigns conducted as part of the Yellow Fever Initiative have had a lasting impact in West Africa, significant under-protected pockets exist at the subnational level. Furthermore, vulnerable populations may have been underserved by previous efforts. Coverage and immunity remain low in many at-risk countries; including those where large-scale preventive campaigns had eliminated the acute risk of epidemics. In West Africa, for example, national vaccination coverage is below the recommended 80% required for herd immunity in eight out of the 13 most at-risk countries even after the completion of vaccination campaigns. Furthermore, where country-level mean coverage exceeds 80% this may mask wide disparities at the subnational level and over time.

Senegal is an example of an at-risk country which has made concerted efforts and impressive progress in reducing the incidence of YF epidemics over the past two decades. The country has increased its vaccination coverage from around 30% in 2001 to 77% in 2014 and 87% in 2016 thanks to a six-year preventive campaign launched in 2002 with the objective of covering a population of 4.5 million people in 22 districts affected by YF. Senegal takes a proactive approach to YF control, drawing on the expertise of local professionals across a range of disciplines. Working with the Pasteur Institute Dakar, the country has established a national sentinel system for arborviruses right down to the
district level. Each district has its own work plan for surveillance and immunization. One particularly simple yet successful element of the system is a monthly newsletter distributed to public health managers. This provides a platform for sharing news and best practice, while fostering both collaboration and a healthy sense of competition between districts to expand coverage. Public health managers also proactively search for pockets of low vaccination coverage and under-served groups to ensure equity of vaccine coverage and make concerted efforts at engagement with civil society and community healthcare organizations. Areas for improvement have also been identified, including the need for a country-level preparedness plan for the eventuality of a large YF outbreak, time needed to mobilize vaccines for reactive campaigns, campaign planning, increasing efforts to ascertain inbound travellers’ vaccination status and expanding cold-chain infrastructure. The country has established a dedicated cold chain capacity team, and progress on this front has been bolstered by recent measles control efforts which have led to expanded cold chain infrastructure and personnel training. Current priorities include improving mobilization of resources for vaccine procurement and strengthening community-based surveillance. Senegal provides an example of effective priority setting, good practice and country ownership which has the potential to be replicated across the African Region.

Nigeria, the region’s most populous country and at high risk for YF, experienced major YF outbreaks in 2017–2018 in a context of ongoing and intensified YF virus circulation. As a result, the country has made three requests for emergency vaccines to the ICG in 2018. The latest outbreak was confirmed in the country on 12 September 2018. Up to 26 August 2018 there were 2,787 total suspected cases, 47 confirmed cases and 10 deaths among confirmed cases (case fatality rate: 21.3%). The country is moving forward with preventive mass vaccination efforts alongside reactive campaigns. Follow-up vaccination of areas of certain states which had not been covered in previous campaigns has also been underway. Preventive mass campaigns were completed in three states in early 2018 and a further 18,651,000 people in another five states are expected to receive vaccination from November 2018 onwards. Achievements include coverage rates of 90% in all but one of its most recent campaigns and the establishment of an emergency operating centre to coordinate YF outbreak response at the national level. Further efforts are required, however, to expand routine vaccination coverage, which is currently below 50% nationally. Ongoing challenges for surveillance include limited capacity for carrying out entomological investigations, insufficient logistics for transporting samples to laboratories, limited laboratory capacity and stock-outs of key reagents. Nigeria currently does not have the capacity to independently confirm a YF outbreak. Samples must be sent
to Dakar, and this can result in delays in confirmation. The country also faces competing campaign priorities such as measles and polio control. There have also been difficulties reaching certain population groups such as adolescents, and certain areas of the country such as Borno State due to ongoing security issues. Lessons learned in recent years include the successful leveraging of polio campaign structures for YF control efforts. The Ministry of Health has also intensified attempts to reach adolescents through celebrity vaccination ambassadors and engagement with secondary education institutions and peer support groups. The country is moving forward with its three-year plan from September 2018 onwards which includes preventive campaigns in four more states in late 2019.

As of 22 August 2018, an outbreak was ongoing in the Republic of Congo in and around the city of Pointe Noire with 192 suspected cases across the country and 1 confirmed case from Pointe Noire. Emergency vaccination has been underway following a request to the ICG.

In the neighbouring DRC there were 454 suspected and 4 confirmed cases in 2017–2018. Challenges for YF control include the country’s large land area, with many populations located in remote areas difficult to reach with routine immunization near its borders with neighbouring countries (many of which are also at high risk of YF epidemics). Other critical areas for improvement include increasing storage and cold chain capacity. Another major challenge includes concurrent Ebola viral disease, circulating vaccine-derived poliovirus, meningitis and cholera epidemics. Despite this, the DRC has achieved a significant increase in population coverage from around 20% in 2004 to nearly 80% as of 2018. The country is working to increase vaccine storage capacity and has just completed construction of a new vaccine distribution hub near Kinshasa. Other achievements include strong political mobilisation, improvements in surveillance and efforts to promote vaccine acceptance and strengthen adherence to routine immunizations schedules. The DRC is also working to improve quality of epidemiological data. Over the period 2019–2023 it is expected that over 100 million doses of YF vaccine will be distributed in the country as part of preventive mass vaccination campaigns. The country also hopes to accelerate the implementation of previously-planned campaigns.

Between January and July 2018, suspected YF cases were also reported in Benin, Burkina Faso, Central African Republic, Chad, Côte d’Ivoire, Gabon, Ghana, Guinea, Mali, Niger, Senegal, Sierra Leone and Togo.
The risk of further yellow fever outbreaks remains across Central, East and Southern Africa where vaccination coverage remains relatively low. The ongoing threat of YF outbreaks underscores the key role of the EYE Partnership in Africa to mobilize partners and strengthen outbreak response, surveillance, laboratory capacity, health system infrastructure and routine immunization. One key element of this effort has included WHO missions to Ghana, Equatorial Guinea, Nigeria, Ethiopia and the DRC over the course of 2018 to support countries’ planning and implementation of the EYE Strategy.
3. Global yellow fever vaccine supply in 2018 and beyond

Partners noted that overall trends in vaccine supply over the next few years appear positive thanks to the significant progress made in market shaping efforts on the part of Gavi and UNICEF SD in support of the EYE Strategy, and manufacturers’ increased confidence in the stability of demand for YF vaccines. Manufacturers are working to increase supply and expand production facilities.

Prior to the EYE Strategy’s inception there was poor visibility on vaccine demand and market shaping effort only occurred on an ad hoc basis. The 2017 EYE Strategy Partners’ Meeting highlighted the need for long-term demand forecasting, and significant progress has been made since then in anticipation of the roll-out of mass immunization campaigns in several countries. Furthermore, during the period 2004–2014 global vaccine supply was consistently below demand and was unstable due to disruptions caused by production issues for some manufacturers and the fact that three quarters of manufacturers’ products were retested for prequalification.

Since 2017, global supply has now begun to approach demand. Global supply was around 135 million in 2018 and it is anticipated that around 150 million doses will be available annually from 2019 onwards (compared with the 75 million available before the EYE Strategy). It is also estimated that nearly 39 million doses will have been made available for preventive campaigns over 2018. Supply estimates have even been revised upwards over the last 12 months and manufacturers have shown greater reliability in meeting their increased output projections. According to the global supply and demand predictions by Gavi, it is expected that global YF vaccine demand will remain within the upper and lower global supply estimates over the period 2019–2024. Going forward, although global supply is set to increase and, over time, will likely meet the vaccine demand scenario set out in the Gavi Yellow Fever Vaccine Roadmap 2017, there is still a risk of stockouts and disruption of routine campaigns if the world is faced with outbreaks of large magnitude (as occurred in 2016). There also is the ongoing need to be able to maintain confidence in the stability of supplies. Based on Gavi’s predictions, this will allow the shipment of 75 million vaccines to Africa annually by 2021 and 135 million by 2026. There is the potential for 1.2–1.5 billion people to receive vaccinations over the next decade including 0.9–1.1 billion in Africa.
As the vaccine supply situation improves over time the focus will shift towards how to use current available supplies in the most targeted way possible to maximize impact. The Supply and Demand Working Group, steered by UNICEF Supply Division (SD), will still play a key role, however, in refining supply forecasts and improving the visibility of supply to facilitate campaign planning. Prequalification of vaccines and regulatory approval in countries receiving vaccines will also remain important issues.

The EYE Strategy partners will continue pursuing market shaping efforts with a view to achieving annual increases in vaccine supply capacity which can add up over the long term. Market shaping involves sending clear signals to manufacturers on the nature of future demand and committing to purchase and make use of the doses they manufacture. Delegates identified the need to articulate ‘credible demand’, based on the number of doses which can be feasibly used in countries within programme constraints (e.g. cold chain capacity). The EYE Programme Management Group (PMG) will continue to work with countries to plan campaign scenarios with current supplies in mind and ensure effective prioritization of their allocation to the most at-risk areas. Credible demand is underpinned by countries’ and donors’ commitments to funding preventive and routine immunization, and UNICEF’s commitment to take up all vaccines offered. Effective contracting for future vaccine supplies in support of the strategy requires not only long-term vision and good faith on the part of donors, but also flexibility from vaccine manufacturers.

“We can’t afford to wait until the next outbreak. We need to be proactive in securing vaccine supply.”

— Dr Socé Fall, Regional Emergencies Director, WHO AFRO Regional Office
3.1. The Gavi Yellow Fever Vaccine Roadmap: Progress towards meeting supply and procurement objectives

Gavi reported on the progress towards meeting its supply and procurement objectives set out in its 2017 Yellow Fever Vaccine Roadmap. These objectives were:

1) Manufacturers are to increase their supply offer to UNICEF SD to over 80 million doses by 2018 and to over 105 million doses in 2021, and to over 440 million doses for the period 2017–2021.

2) During the 2017–2021 period, no manufacturer experiences a disruption of more than 15% per year on its expected supply output, and no vaccine is suspended from prequalification.

3) The UNICEF SD weighted average price in 2020 is ≤ the target value (confidential).

4) The overall YF vaccination wastage rate is well understood and less than 25% by 2020 (≤40% routine, ≤10% campaigns), without reducing coverage.

Gavi reported to the EYE Strategy partners that the first target of increasing manufacturers’ global supply offer to UNICEF SD to 80 million doses by 2018 has nearly been achieved, and that, based on current trends, annual supply is expected to increase through 2020 and exceed 105 million doses by 2021. Gavi also reported that the second and third targets have now been met. Further progress is still needed, however, towards meeting Gavi’s fourth target of reducing vaccine wastage to less than 25% overall by 2020. While this suggests the need for an analysis of the programmatic suitability of different vaccine presentations as a way to reduce waste, technical partners emphasized that reducing wastage should not come at the expense of patient safety and missed opportunities for vaccination—particularly for those most in need.
3.2. Vaccine manufacturer updates

There are currently four prequalified manufacturers: Bio-Manguinhos, Sanofi Pasteur, Pasteur Institute in Dakar and Chumakov. Manufacturers highlighted the need for increased frequency of communication with the PMG to gain a fuller picture of credible demand into the future as the Strategy develops.

Bio-Manguinhos (Brazil) is investing in improvements in packaging and labelling, scaling up production of dilutants, and measures to extend vaccine shelf life. Plans have also been drawn up for a new production facility that is expected to supply doses for export and the company is seeking investment partners.

Sanofi Pasteur (France) has also been proactive in expanding production capacity, which has doubled since 2016 in response to the major outbreaks in Angola and DRC.

The Pasteur Institute in Dakar (Senegal) is expected to increase vaccine output by 20% by 2020 as it moves forward with its plans to implement a fully-automated production line. Improvements have also been applied to the facility’s power supply and production equipment.

Chumakov (Russia) is in the process of renovating its primary production facility following investment from the Russian government. The first phase of the project is expected to be completed by 2020.

Vaccine manufacturers expressed that they would view a higher level of interaction with the EYE Strategy partners as valuable, and that this could be facilitated through quarterly updates. Stronger communication would give manufacturers a stronger awareness of country needs in terms of quantities of doses, and when countries can accept vaccine deliveries. This in turn would assist in production planning and reduce the likelihood of having to store large volumes of vaccine for extended periods before being dispatched.

YF vaccine supplies remain under pressure due to competing priorities. While Brazil rolls out its large scale vaccination programme, and countries such as Nigeria and DRC are seeking to accelerate the implementation of planned preventive campaigns, a growing number of children in the PAHO Region who have been missed by routine immunization require catch-up vaccination.
4. Governance

EYE's governance's structure is based on strong partnerships and multi-layered commitment on all levels, well-orchestrated collaboration and communication between partners, and streamlined decision-making, implementation, monitoring and evaluation to drive the Strategy forward with a comprehensive global approach. A key achievement of the Strategy since its inception is that its governance structure, first proposed in 2017, is fully operational. The terms of reference of the key working groups are defined, and they and the PMG are moving forward with the Strategy’s implementation.

This governance structure comprises three elements. These include strategic direction, guided by the EYE Leadership Group (LG); implementation, performed by the PMG (comprising representatives from WHO, Gavi and UNICEF) in concert with regional focal points; and input from contributing partners including technical working groups. All these activities are coordinated by the EYE Secretariat.

Figure 2. EYE governance structure
Following agreement by partners to move forward with the establishment of the Immunization Operational Guidance Working Group and the expansion of activities proposed by the Supply and Demand Working Group, the EYE Strategy is now complemented by four technical working groups, and the meeting highlighted the wide scope for cooperation between them.

Stakeholders emphasized the need for close cooperation between the PMG and partners at the country level to guide immunization strategies and provide operational expertise as the Strategy is developed and mass and routine immunization are rolled out. Effective planning at the country level and successful requests for Gavi funding in collaboration with the PMG can strengthen the demand signal for the production of more vaccines and drive further progress towards expanding coverage. Continuing feedback from the PMG to the EYE partners will ensure that the Strategy’s priorities are driven by operational needs and realities.
5. Technical priorities & emerging issues

As the Strategy develops and the epidemiological situation changes over time, so will the Strategy’s technical priorities.

The EYE Strategy’s current technical priorities are:

• Ensuring effective outbreak response to limit morbidity, mortality and the risk of spread;
• Accelerating and enhancing the implementation of preventive mass vaccination campaigns;
• Expanding and improving performance of routine immunization in high risk countries;
• Guiding effective prioritization of resources at a global level through assessment of YF risk and disease burden; and
• Enhancing surveillance and laboratory capacity.

The meeting included presentations from the Risk Analysis, Immunization Operational Guidance and Laboratory working groups, which highlighted the latest developments in addressing the Strategy’s priorities as it moves towards supporting the roll-out of mass preventive and routine immunization in a number of countries. Delegates were also updated on the latest research covering fractional dosing and YF vaccine co-administration, and how they could be potentially leveraged towards achieving the strategy’s objectives.

5.1. Country risk assessment

Globally, there are 40 countries at high risk of YF outbreaks. Risk varies markedly both between countries and sometimes within countries. Key factors influencing the degree of YF outbreak risk include presence of the virus, presence of *Aedes*, *Haemogogus* and *Sabethes* vectors, presence of susceptible human and non-human primate reservoirs, rainfall, vegetation, temperature and land elevation. All these factors interact with one another and may evolve over time.

As a global strategy, EYE must assess risk at a global level to inform future priorities for guiding decisions on the allocation of global vaccine supplies. These priorities and decisions must be impartial and evidence-based, not only to maximize the Strategy’s effectiveness at achieving its objectives, but also to engender trust among its stakeholders. The Risk Analysis and Modeling Working Group was established to lead on categorization of YF risk as part of the Strategy in close collaboration with experts and building on the previous Yellow Fever Initiative.
Its key objectives are:

• To evaluate risk of YF at the national and local level,

• To guide prioritization of YF immunization activities based on risk assessments.

In December 2017 the working group held a meeting to discuss alignment of existing risk maps to create a ‘mother map’ which would place countries into four risk categories ranging from no risk to high-risk while accounting for differences in risk at the sub-national level. Factors used to define risk were identified, including previous outbreaks, number of reported cases, previous vaccination campaigns, YF seroprevalence and presence of vectors.

To fully characterise risk and refine assessments it is necessary to identify all the relevant variables. Furthermore, criteria for quantifying risk must be transparent and comparable across different countries and regions. These tasks are complicated, however, by the fact that drivers of YF risk may differ across regions and that quality of data for measuring them is variable across different countries. Specific technical questions include, local vaccination coverage, population vulnerability, the potential size of outbreaks, and the capacity of health systems to detect and manage outbreaks after they occur, and, in the PAHO Region, competence of local vectors for YF. When prioritizing campaigns, YF risk assessments must therefore be considered alongside countries’ competing priorities and capacity to detect and respond to YF outbreaks. Delegates also identified mapping of non-human primate reservoirs, particularly in the PAHO Region, as a future research need to further refine risk estimates.

The Risk Assessment Working Group will meet to discuss and review criteria for defining risk, and which variables should be considered in collaboration with the PMG and other working groups. It will also work to identify critical data gaps at the national and sub-national levels. In November 2018 the PAHO Regional Office will host a YF risk assessment and vaccine demand workshop in Peru. This will present the working group an opportunity to obtain feedback from stakeholders and country partners. The end goal of these efforts will be to finalize the ‘mother map’ and develop a prioritization matrix to guide YF vaccine allocation as the Strategy develops and to tier responses at the sub-national level.

“The EYE is a global strategy and therefore needs a global perspective on risk and resource allocations.”

— Dr Laurence Cibrelus Yamamoto, EYE Secretariat Lead, WHO
Finally, risk assessments cannot be static: they must be periodically revised to ensure an up-to-date picture of outbreak risk. New and unforeseen developments can also influence risk of YF transmission, for example the development of extractive industries and population movements in the wake of conflicts or other crises. Unexpected outbreaks also point to the need for flexibility in risk assessment. In the longer term, the working group will reassess risk analyses on a routine basis and consider evaluations to collect key missing data. Where data do not exist, the working group will employ modeling to improve risk assessments where gaps exist in the available data. It will sustain engagement with the EYE Secretariat and other working groups to ensure that risk analyses are relevant to the needs of the Strategy and used effectively in prioritizing campaign needs.

5.2. Surveillance and laboratory capacity

In the PAHO Region, YF case confirmation relies on a tiered network of national laboratories. The Arborivirus Diagnosis Laboratory Network of the Americas (RELDA) comprises 30 national laboratories in 26 countries with full capacity for molecular detection of at least four arboviral diseases. The region has four reference laboratories with the capacity to confirm YF cases, which will be expanded to six in the coming years. The WHO AFRO Region, meanwhile is currently served by one reference laboratory based at the Pasteur Institute in Dakar, which is expected to be joined by two more by mid-2019 as efforts are underway to strengthen the Region's laboratory network.

Laboratory capacity refers not only to laboratory facilities, but also the existence of other physical and organizational infrastructure to facilitate delivery of samples and availability of critical reagents and human resources. The EYE Strategy calls for the strengthening laboratory diagnostic capacity in all aspects, particularly in Africa where the need is most acute.

The EYE Laboratory Technical Working Group was set up to inform the EYE Strategy on critical elements such as:

- Strengthening capacity and capability at national and regional levels based on needs,

- Increasing the availability of high-quality diagnostics,

- Improving information sharing between laboratories and national partners,

- Strengthening quality assurance and quality control mechanisms to ensure results are reliable,

- Engaging governments and other partners to advocate for the importance of laboratory capacity and sustainable funding for laboratory and surveillance activities.
Key issues raised included alignment of testing protocols for YF laboratories and financial and human resources. Furthermore, serological testing, which is primarily employed at the national level in the African Region, is vulnerable to cross-reactivity between YF and other flaviviruses which may give false-positive results. To address this, the Laboratory Working Group will evaluate the potential for the introduction of additional diagnostic tools (e.g. increasing number laboratories capable of performing molecular testing (PCR) and whether commercially-available test kits for serologic and ELISA may present a viable alternative.

Near-term objectives include finalizing the new common laboratory testing algorithm for the African Region by the end of 2018 and continuing efforts to upgrade national and regional laboratories with a view to finalizing the nomination of the Uganda Virus Research Institute (UVRI) as a regional reference laboratory by end of 2018 and the Pasteur Centre in Cameroon (CPC) by mid-2019. The working group will hold a meeting on the 11–12 December 2018 to discuss both these issues, in addition to drafting its work plan for the following 12–18 months.

The EYE Strategy Partners’ Meeting was held back-to-back with the EYE proposal for lab capacity and network strengthening in Africa on 14 September (reported in Annex IV). This proposal, due to be submitted to the Gavi Programme and Policy Committee by 19 October 2018, calls for approximately 12 million USD of funding to enhance laboratory capacity and strengthen the laboratory network in the Region. Its scope covers a range of activities, including procurement of reagents, supplies and equipment; technical assistance; quality assurance and quality control; international sample transportation; and very limited human resources in the form of laboratory coordinators (one at AFRO and one at WHO HQ) for the period 2018–2020.

“Without effective surveillance, the EYE is blind.”

— Professor Oyewale Tomori, President, Nigerian Academy of Science
5.3. Immunization

Partners endorsed the establishment of the new Immunization Operational Guidance Working Group.

The Immunization Operational Guidance Working Group's two primary tasks are:

- To provide guidance on approaches for increasing YF vaccination coverage, particularly routine coverage,

- To provide specific operational guidance (e.g. for different age groups) for targeting campaigns and on screening of YF vaccination status).

While it will work to provide countries with guidance on the introduction of YF vaccine into routine immunization schedules, it will also leverage its significant technical and operational expertise in dealing with countries' operational questions, including how to explain priorities to stakeholders at the country level, which age groups should be targeted and the process for screening vaccination status in advance of catch-up campaigns. The working group will also support the formulation of policy and research questions. Delegates highlighted the need for advice to be made more accessible, succinct and relevant for national partners.

Its proposed terms of reference include:

- Assisting countries in introducing routine YF vaccination,

- Advising countries on boosting coverage,

- Responding to operational questions from countries,

- Undertaking a review of available evidence on target age groups, immunization of pregnant and lactating women, and co-administration with other vaccines while ensuring that information is made readily available to countries.

A number of challenges for expanded routine immunization were identified, including limited health system capacity in many at-risk countries, patient education and social engagement, availability of information for stakeholders at the country level, and the stability of vaccine supply. The root causes of low routine immunization are often not specific to YF and must be addressed at the country level nonetheless. While the working group will engage country partners to overcome these, the need was also highlighted...
for regular communication with the Supply and Demand Working Group. Delegates discussed the ongoing issue of recording of immunization status, and the potential for the introduction of electronic vaccination databases as a way of minimizing duplication of previous efforts and directing available doses to those most in need.

The meeting also raised the issue of barriers to vaccine uptake and determinants of coverage in routine immunization, including vaccine availability, parental safety concerns, availability of reliable information, and maternal education and social engagements.

Senegal was highlighted as a key example of a success story in terms of effective human resources management and training, integration of services, data management and campaign planning. The country is actively continuing to use YF vaccine as part of routine schedules at 9 months alongside measles and rubella vaccines.

Finally, participants discussed the role mass vaccination campaigns can play in laying the groundwork for expanded routine immunization. They also highlighted key ingredients for success in introducing routine immunization, including streamlining of bureaucracy and registration of vaccines, comprehensive training of personnel before roll-out, involvement of local stakeholders, and public education efforts to ensure the vaccine is accepted. Making the launch of immunization an event in itself presents the opportunity for advocacy and awareness-raising.

Over the coming months the Immunization Working Group will finalize its composition, including representatives from UNICEF Programme Division, WHO HQ and Regional Offices, the CDC and other organizations. It will also agree on its TORs and mechanisms of work moving forward. The group will hold one or more face-to-face meetings per year, along with quarterly and ad hoc teleconferences. The Immunization Operational Guidance Working Group is set to play a key role in driving progress towards meeting the EYE Strategy’s objectives, particularly as Sudan, Uganda, South Sudan, Ethiopia and Brazil prepare to introduce routine immunization and Kenya introduces routine immunization sub-nationally over the next year.
5.4. Fractional dosing

In July 2016, the WHO issued a new recommendation that one-fifth of the regular dose of the yellow fever vaccine could be used for emergency outbreak response when there is a shortage of vaccine. In August 2016, in the context of major concurrent outbreaks in Angola and the DRC, which contributed to major YF vaccine shortages and resulted in global stockouts on multiple occasions, fractional dosing was employed with success to vaccinate 7,586,400 people in response to an urban outbreak of YF in Kinshasa, DRC. In January 2018, Brazil initiated a mass vaccination campaign using standard and fractional dosing targeting more than 25 million people. Until data relevant to specific subgroups becomes available, children aged <2 years, pregnant women, and individuals known to be HIV-positive should preferentially be vaccinated using a standard dose of yellow fever vaccine.

Two presentations discussed the issue of fractional dosing safety and effectiveness. The first was conducted by the Centers for Disease Control and Prevention (CDC) on 716 participants who had received 1/5th fractional doses in Kinshasa in 2016 with follow-up at 28–35 days. Its results showed that seroconversion had occurred within one month in 98% of all recipients with no previous immunity. The seroconversion rate was lower among those aged under five years, however. It also showed that 66% of participants who were seropositive at baseline had a four-fold increase in antibody titre. The Fundação Oswaldo Cruz (Fiocruz) presented a study on five different YF vaccine doses, showing that only the two lowest doses less than a 1/47th fractional dose had lower rates of seroconversion than the full reference dose. At eight years after follow-up, it was found that at least 80% of the subjects who had seroconverted after yellow fever vaccination showed seropositivity comparable to that of the full dose regardless of the dose they had received (even down to a 1/886th dose).

Together, these studies point to the high potential efficacy of fractional dosing effective at providing protective immunity, and its viability as an option for outbreak response during severe vaccine shortages. Although no new recommendations from the SAGE are anticipated in the near future, the EYE partners and Immunization Operational Guidance Working Group will monitor the evidence base as it evolves. Despite the evidence of its potential efficacy, immunization by fractional dosing remains insufficient to entitle recipients to a yellow fever certificate valid for international travel.

Another significant issue for campaigns employing fractional dosing is that of communication. One challenge noted during Brazil’s mass preventive campaign has been the need to overcome hesitancy and secure acceptance from both health personnel
and civil society. Clear messaging is essential to minimize the risk of circulation of false information. In addition, messaging must be flexible and adapted to react to changes in the wider social and political environment. For example, in Brazil, the Carnival and national holidays slowed down the vaccination campaign and decreased the population’s perception of YF risk and demand for vaccine uptake.

Another challenge is organizing the logistics for a rapid campaign over a short time period, in which health services must be prepared to administer both standard and fractional doses. This can be hampered by difficulties in assessing true vaccination coverage and gaps in microplanning, and specific strategies are required to reach target groups such as young males and mobile workers. The need to procure large quantities of 0.1 ml auto-disable syringes specifically for fractional dosing also posed a significant challenge. Overall, Brazil’s experience highlights the need for rapid coverage monitoring and effective registry systems.

5.5. Yellow fever vaccine co-administration in routine settings

The EYE regional kick-off meeting in Abuja in April 2018 provided new impetus to the expansion of routine immunization which has been ongoing since 2016. Several countries in Africa are now in the process of introducing routine YF immunization as a result of the Strategy.

Encouragingly, the gap between YF routine coverage and that of the first dose of measles-containing-vaccine (MCV1) is closing and currently only two of 21 African countries with data had a vaccination coverage gap of over 10% between YF and MCV1. While there has been some convergence of coverage rates for YF and measles in recent years, this could be happening at a faster pace and accelerated through co-administration. The SAGE currently recommends that the YF vaccine may be co-administered with other vaccines. The 2013 SAGE working group on vaccine co-administration identified 28 studies involving co-administration of YF vaccines. All but one of these studies found no evidence of interference and the review identified no safety concerns or compromised immunogenicity among vaccine recipients. Although seven studies with a measles vaccine found no impact on immune response, one study on co-administration of MMR and YF vaccines from Brazil (2011) showed decreased immune response to mumps, rubella, and YF among children aged 12–23 months. Since then, new data was presented to the SAGE in 2018. While one study from France (2017) showed some evidence of interference when YF and MMR vaccines were co-administered, studies conducted in the Gambia
(2014) and Argentina (2018) found no interference. Overall, these two studies do not give sufficient justification for changing this recommendation for co-administration with the MMR vaccine.

Decoupling the administration of MMR and YF vaccines represents missed potential opportunities for vaccination. This has been shown in Argentina, Colombia and Panama, where YF coverage among children fell temporarily when MMR and YF vaccinations were moved apart in routine immunization schedules. Experiences in the PAHO Region point to synergies that can be achieved by sharing resources between YF and other campaigns such as for measles and polio—particularly when targeting remote or previously underserved areas. Follow-up measles vaccination campaigns have also presented opportunities not only to reach unvaccinated children, but also to reach other family members.

There are a number of advantages and disadvantages to co-administrate vaccines in mass preventative campaigns and routine immunization campaigns.

Advantages and opportunities:

- Cost savings,
- Time savings for both personnel and caregivers,
- Unified communication,
- Fewer missed opportunities to increase coverage.

Disadvantages and challenges:

- Some questions remain over the effectiveness of co-administration and potential for lower immunogenicity;
- More time needed per patient: although co-administration saves time overall there is a need to plan for a longer campaign;
- Logistical complexity;
- Training needs;
- The need to engage healthcare providers to secure acceptance.
On balance, co-administration of YF vaccines can be beneficial, but the disadvantages highlight the need for better planning (including alignment of coverage targets), logistics, training and supervision to unlock their full potential. Co-administration may be particularly relevant for remote settings where the major challenge is delivery of vaccines. The human resources requirements, additional planning and upfront costs associated with combined campaigns can be a major barrier in resource-poor settings, however. As with fractional dosing, partners need clear recommendations on campaign planning and budgeting, in addition to how to present combined campaigns when applying for funding from donors. Delegates identified the PMG as having a key role in assisting individual countries.

Specific guidance to countries on co-administration will depend on immunization coverage for YF and other vaccine-preventable diseases. Where gaps exist, for example between measles and YF coverage, this represents an opportunity to increase YF coverage by benefitting from the immunization infrastructure already in place. At the same time, efforts at expanding preventive and routine coverage for YF can draw on momentum from campaigns for other diseases. Finally, where progress towards expanding coverage for diseases such as measles has plateaued (as has occurred in some countries in recent years) co-administration can be promoted as an overall strategy for tackling vaccine-preventable diseases.

“Countries have successfully administered the measles vaccine in new generations and the same needs to be done for yellow fever. Progress has been made in the last years, and the gap between measles and yellow fever vaccination is closing.”

—Dr Kaushik Banerjee, EYE Secretariat, WHO
6. The EYE Country Guidance Toolkit

In late 2017 the EYE partners identified the need for specific country-level guidance to accelerate the Strategy's implementation and update partners on the ground on scaled-up approaches to rolling out immunization. It was agreed that this would take the form of a set of guidance summaries targeted at country-level audiences including ministry of health personnel responsible for planning and coordinating YF control activities, and other public health partners in the field. The Toolkit will be organised around key issues relating to each of the Strategy's three primary objectives: protecting at-risk populations, preventing international spread, and containing outbreaks rapidly. In addition, it will cover three cross-cutting themes: identifying and reaching vulnerable populations; advocacy, communication and social mobilisation; and monitoring quality and measuring vaccination coverage.

The Toolkit's objectives are:

• To provide practical and easy-to-use guidance for implementing YF control activities at the country level;

• To provide information on sources of technical and operational support that countries can access, including EYE partners for expertise in routine and mass vaccination; and

• To orient country partners towards examples of best practice.

The Toolkit will comprise succinct summaries of key steps for core Strategy activities. While the Toolkit is not intended to be fully comprehensive, it will refer country partners to a range of resources for more detailed guidance.

Summaries will include mechanisms for working most effectively with Gavi to ensure rapid acceptance of funding applications for eligible countries, gathering key data for monitoring and evaluation of outbreak preparedness, and making emergency requests to the International Coordinating Group on Vaccine Provision to ensure timely release of emergency vaccines. It will break down complex, technical issues into their key components. For example, on the topic of fractional dosing for reactive vaccination campaigns, it will address not only the potential and limitations of this approach, but also provide clear advice on communication strategies for different target audiences to ensure acceptance among the public and healthcare workers.

Stakeholders from ministries of health and other organisations at the country level in particular were solicited for their input to ensure that guidance is targeted and relevant, and to comment on the clarity of the structure and content. Participants were requested to provide feedback by the end of October 2018 and it is expected that the full Toolkit will be published in early 2019.
7. Discussion

Major themes that emerged were the need to emphasize health system strengthening, the importance of routine immunization, and the role of country ownership in catalysing progress towards eliminating YF epidemics. The need to improve readiness in urban areas to protect populations at source was also highlighted due to the unpredictable nature of outbreaks in recent years. The underlying risk of YF outbreaks remains and immunization coverage remains below recommended levels in several countries in the African Region. The increase in global YF vaccine supplies since the Strategy’s inception is a positive development. It is crucial for the Strategy’s success for partners to maintain confidence in supplies, and commitment to continuing market shaping efforts. There is a shift in the emphasis of the EYE Strategy towards supporting countries to accelerate roll-out of preventive and routine immunization, and how to best utilize vaccine supplies to maximize impact. These questions are now beginning to be addressed by the EYE Strategy working groups.

Moving forward, the EYE Strategy must develop approaches to: i) define and measure global risk to drive country prioritization and ensure equitable resource allocation; ii) enhance laboratory and surveillance capacity where the need is most acute; and iii) support the expansion of routine immunization coverage. Delegates emphasized the need for a flexible and opportunistic approach to pursuing all three of these priorities. Outbreaks, should they occur, are also an opportunity to focus attention and apply pressure at the political level to make YF control a priority. In addition, leveraging combined campaigns presents an opportunity to reach populations with low YF vaccine coverage.

The experiences of previous initiatives for other controlling infectious diseases (e.g. measles, meningitis and polio), and examples of best practice in surveillance and expansion of preventive and routine immunization at the country level, can provide lessons for YF control efforts going forward. Senegal, the host country of the meeting, has made sustained efforts towards eliminating YF epidemics which are reaping long-term dividends. The country’s experience highlights not only the importance of effective integrated surveillance right down to the community level and the benefits of investment in surveillance and laboratory capacity, but also results that can be achieved through commitment at all levels to preventing and eliminating outbreaks.

“Leadership and accountability at the country level are absolutely key. This is applicable to all [WHO] Regions.”

— Dr Kaushik Banerjee, EYE Secretariat, WHO
The PMG has a vital role to play in advocating for the EYE Strategy directly to priority countries. The PMG can advocate for commitment from national and sub-national partners, support proactive identification of bottlenecks and constraints delaying roll-out of vaccination, and promote health system strengthening.

Together, the diverse elements of the EYE Strategy jointly contribute to the translation of YF risk into demand for vaccines, and to the implementation of preventive and routine vaccination in endemic countries. Demand is driven by awareness of YF risk as a result of effective risk analysis and effective surveillance and laboratory networks. Demand for vaccines is translated into increased vaccine supply through market-shaping efforts, commitments from funders and articulation of ‘credible demand’. Expanded vaccine supply, alongside effective supply forecasting and prioritization, allows greater scope for planning of mass preventive campaigns and expansion and strengthening of routine immunization. Effective planning at the country level, with the input of the PMG, is vital to ensuring campaigns maximize vaccination coverage and reach populations most in need. Finally, strong implementation is assured through country ownership of vaccination campaigns, strengthening overall health system capacity, developing human resources and overcoming operational challenges such as limited cold chain capacity. To achieve the Strategy’s objective of eliminating the threat of YF epidemics by 2026, all four technical working groups, the PMG, and the EYE Secretariat, in addition to donors, manufacturers, academic partners and individual countries, must work in concert while playing their respective roles to translate awareness of YF risk into increased immunization coverage on the ground.

“Understanding how the EYE Partnership can best support countries to have ownership in the implementation of the strategy is crucial for its success.”

— Dr Laurence Cibrelus Yamamoto, EYE Secretariat Lead, WHO
8. Action points

The EYE Secretariat identified the following action points for the coming year, which were agreed upon by consensus:

• The PMG is to compile a work plan to be completed ahead of the upcoming EYE Strategy Retreat in Geneva on 19–20 November 2018 for input from Strategy partners.

• The complete work plan will be finalized by mid-January 2019.

• It will set out a clear timeline and clarify the roles and responsibilities of each EYE partner.

• The EYE Secretariat will move forward with the establishment of the Immunization Operational Guidance Working Group, draw up a proposal on its composition and define its terms of reference and mechanisms of work.

• All working groups are to set out their milestones for the next 6–12 months.

• EYE partners will provide their input on the EYE Country Toolkit by the end of October 2018.

• The PAHO Regional Office will hold a YF risk assessment and vaccine demand workshop in Peru in November 2018.

• The EYE Secretariat, WHO and its partners will continue to support ongoing progress towards establishing a total of three regional reference laboratories in the African Region.

• The EYE Secretariat and partners will provide support for an application to Gavi for funding for enhancing laboratory capacity in the African Region.

• The PMG partners will continue to support the implementation of ongoing mass vaccination campaigns in Nigeria, Ghana and Sudan to reach over 35 million people by the end of 2018.

• The EYE Secretariat, together with partners, will assess the need and identify potential funding sources for YF focal points in at-risk countries.
8.1. Working group action points

The Supply and Demand, Risk Analysis and Laboratory working groups set out their specific objectives for the coming year:

Supply and Demand Working Group

• Arrive at a common consensus on routine and campaign vaccine demand and allocation at the global level.

• Improve communications between the PMG and manufacturers by setting up dedicated meetings.

• In collaboration with the Immunization Operational Guidance Working Group, analyze the suitability of different vaccine presentations (i.e. 2-, 5-, 10- and 20-dose vials) for different scenarios and settings with a view to reducing wastage.

• Continue to make progress market shaping efforts to expand global vaccine supply.

Risk Analysis Working Group

• Establish the criteria used to define YF risk at the global level, gather feedback from partners including the AFRO and PAHO Regional Offices and individual countries, and define which criteria are most important.

• Set up routine working group meetings going forward with a view to refining and reassessing YF risk in response to changes in the epidemiological situation.

• Collect and analyze existing data to evaluate YF risk at the country and sub-national level, using modeling where there are currently gaps in the available data.

• The working group will draw up prioritizations of vaccine needs for different potential risk scenarios.

Laboratory Working Group

• Initiate a development plan for a three-year strategy to build laboratory capacity in the African Region.

• Finalize the laboratory capacity investment proposal to be submitted to the Gavi Programme and Policy Committee in October.
8.2. Key priorities

The delegates also acknowledged the following priorities for the EYE Strategy’s work going forward:

- Fostering communication among Strategy partners to create synergies, leverage EYE’s critical mass of expertise, improve coordination and clearly define their respective roles and responsibilities.

- Stepping up engagement with individual countries, securing political commitment, promoting country ownership and pushing for health system strengthening.

- Strengthening the PMG’s role in advising individual countries on campaign planning, technical issues and making applications for vaccination campaign funding.

8.3. Upcoming milestones

November 2018: The PAHO Regional Office will hold a YF risk assessment and vaccine demand workshop in Peru.

November 2018: The PMG will hold its Retreat in Geneva and draft a work plan for the next 12–18 months.

December 2018: The Laboratory Working Group will hold a meeting and finalize its combined laboratory testing algorithm for the African Region by the end of the year.

End 2018: Preventive mass vaccination campaigns are expected to have reached over 35 million people in Nigeria, Ghana and Sudan while Kenya will have introduced the YF vaccine into routine immunization schedules sub-nationally.

Early 2019: The final version of the EYE Country Guidance Toolkit will be made available to country-level guidance on rolling out YF immunization.

Mid-2019: The African Region will be home to three YF reference laboratories with the addition of the Uganda Virus Research Institute (UVRI) and the Pasteur Centre in Cameroon (CPC) alongside the Pasteur Institute in Dakar.

Late 2019: The next EYE Strategy Partners’ Meeting is planned to take place in Brazil.
End 2019: Preventive mass vaccination campaigns are expected to reach nearly 60 million people in Nigeria, Ghana, Sudan and the DRC while Sudan and Ethiopia will have applied for the YF vaccine introduction into routine immunization schedules.

End 2020: Five preventive campaigns are expected to have been completed in Nigeria, the DRC, South Sudan, Ethiopia and the Republic of the Congo. Together these campaigns will target over 80 million people.
9. Conclusion

The meeting’s participants praised its open and dynamic sessions, which gave partners further impetus to drive the Strategy to move forward in terms of governance, implementation and planning to support countries. The discussions laid the foundation for the next stage in the Strategy’s development and set clear priorities for the months ahead. It was also an opportunity to recognize the Strategy’s achievements to date and discuss how to build on them.

The meeting brought together representatives from a wide diversity of agencies, partners, country representatives, vaccine manufacturers and donors. Although each brought different perspectives and expertise to the table, all were united in their long-term commitment to ending YF epidemics. Manufacturers, whose engagement and cooperation is key to securing the vaccine supplies needed for the Strategy’s success, shared their perspectives and plans for expansion of vaccine production in future years. The meeting also focused minds on how the strategy can bring together the various partners and stakeholders to achieve synergies in their work.

The Strategy has made significant progress since its inception in 2016, and partners noted its positive trajectory. Additional highlights included the presentation of the EYE Country Guidance Toolkit, which was presented to country representatives and Strategy partners for their final input, and updates on the significant steps which are being taken to increase capacity and strengthen the laboratory network in the African Region such as the establishment of two new regional reference laboratories. The EYE Governance structure is now operational, and the Strategy is currently on track to meet its targets. Two achievements of the meeting include the establishment of the Immunization Operational Guidance Working Group and the expansion of the Supply and Demand Working Group’s role. All four working groups are now progressing with their work plans and are setting out their objectives for the coming 12–18 months. By the end of 2018, more than 100 million people will have been protected against yellow fever through reactive, preventive and routine immunization. This success is underpinned by the growth and stability of global vaccine supplies, and this has been at least in part a positive result of vaccine market shaping efforts and strong engagement with manufacturers.

These successes set the stage for further progress. Moving forward, effective collaboration between global and national partners, and country ownership of preventive and routine immunization programmes in particular, will be key to unlocking the Strategy’s full potential and to turn the linear progress achieved to date into exponential gains. As a result of all these efforts, 1.2–1.5 billion people globally are expected to be immunized over the next decade with the support of the Strategy. By 2026, all high-risk countries are expected to have completed preventive mass vaccination campaigns.
The annual EYE Strategy Partners’ Meeting in Dakar was a successful opportunity to bring together a critical mass of committed partners, experts and country representatives to enable the strategy to move forward in terms of governance, implementation and planning to support countries.

Our ultimate goal is ambitious and we will need continuous support from partners and countries to eliminate yellow fever epidemics by 2026. With a concerted effort, it is possible.

— Dr Laurence Cibrelus Yamamoto, EYE Secretariat Lead, WHO
Annexes
Annex I: List of participants

<table>
<thead>
<tr>
<th>Name</th>
<th>Organization</th>
<th>Email</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kaushik Banerjee</td>
<td>EYE Strategy</td>
<td><a href="mailto:banerjeek@who.int">banerjeek@who.int</a></td>
</tr>
<tr>
<td>Viviane Bianco</td>
<td>EYE Strategy</td>
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</tr>
<tr>
<td>Sylvie Briand</td>
<td>Director IHM</td>
<td><a href="mailto:briands@who.int">briands@who.int</a></td>
</tr>
<tr>
<td>Laurence Cibrelus</td>
<td>EYE Strategy</td>
<td><a href="mailto:cibrelusl@who.int">cibrelusl@who.int</a></td>
</tr>
<tr>
<td>Jennifer Horton</td>
<td>EYE Strategy</td>
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</tr>
<tr>
<td>Mick Mulders</td>
<td>WHO HQ</td>
<td><a href="mailto:muldersm@who.int">muldersm@who.int</a></td>
</tr>
<tr>
<td>William Perea</td>
<td>IHM</td>
<td><a href="mailto:pereaw@who.int">pereaw@who.int</a></td>
</tr>
<tr>
<td>Kelly Ronan</td>
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<td>Raphael Slattery</td>
<td>WHO/HQ</td>
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<tr>
<td>Eduardo Vargas Garcia</td>
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<tr>
<td>Blaise Bathondoli Kambale</td>
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<td>Kerstin Bycroft</td>
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<td>Annick Dosseh</td>
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<tr>
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<td>WHO/RED Director</td>
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<tr>
<td>Mamoudou Harouna Djingarey</td>
<td>WHO/AFRO</td>
<td><a href="mailto:djingareyh@who.int">djingareyh@who.int</a></td>
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<tr>
<td>Dr Anne Achoribo</td>
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</tr>
<tr>
<td>Dhamari Naidoo</td>
<td>WHO/Nigeria</td>
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</tr>
<tr>
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</tr>
</tbody>
</table>
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Shaza M Ahmed
UNICEF SUDAN
Annex II:
Meeting agenda

Eliminate Yellow Fever Epidemics (EYE) Strategy 2018 Annual Partners Meeting
11-13 September 2018, Dakar, Senegal (King Fahd Palace Hotel)
Hosted by UNICEF WCARO
Organized by the World Health Organisation, UNICEF and Gavi Secretariat

Objectives:
• To review and discuss among global, regional and country EYE partners, YF epidemiology and key issues related to the implementation of EYE strategies. (sessions 1 & 2)
• Strengthen partners engagement (cross-cutting, session 2)
• To enhance priority countries engagement (sessions 1 & 4)
• To assure continued supply of YF vaccine through improved demand forecasting and understanding of YF vaccine manufacturers production capacity and viewpoints (session 3)
• To review and discuss the EYE strategy future plans and the way forward (session 5)

Expected outputs:
• Document successes, lessons learned, best practices, constraints and solutions in the implementation of the EYE strategy to increase routine YF vaccination coverage, introduction of routine YF vaccination in high risk countries, implementing preventive mass vaccination campaign as well as timely reactive campaigns for outbreaks;
• Develop 180d multi-partner action plan with clear roles, responsibilities, and deliverables;
• As accurate as possible 2 year forecast of YF vaccine supply.

Rapporteur: Sol Richardson (WHO consultant)
Translation services provided: French to English, English to French. Ad-hoc translation to Portuguese and Spanish available upon request.

WebEx Link:
https://who.webex.com/who/j.php?MTID=m8d79990db8fd061cd55c3edd88e87d7e
Meeting number: 494 124 118
Password: 12345A

Dropbox link:
https://www.dropbox.com/sh/l0cycugewza2p3s/AABFS0wzzFysXP7mjm5gwoUa?dl=0
Includes:
- Logistical notes
- Meeting documents and pre-reads
**DAY 1 – Tuesday, 11 September 2018**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:00 – 8:30</td>
<td>Registration</td>
</tr>
<tr>
<td><strong>Session 1: Opening &amp; Epidemiological update – Chair: Socé Fall (WHO)</strong></td>
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<tr>
<td>Objectives:</td>
<td>- Update on YF epidemiology and changing dynamics of YF infection</td>
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<td>- Provide stimulus to accelerating EYE strategy engagement and</td>
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<td></td>
<td>implementation by discussion forum with leading technical experts</td>
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<tr>
<td>8:30 – 9:00</td>
<td>Welcoming remarks &amp; introduction of participants Senegal MoH representative &amp; WHO / UNICEF RD</td>
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<tr>
<td>9:00 – 9:10</td>
<td>Overview of meeting objectives &amp; expected outcomes</td>
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<tr>
<td>9:10 – 9:15</td>
<td>Global Overview of YF Epidemiology EYE Secretariat</td>
</tr>
<tr>
<td>9:15 – 9:30</td>
<td>Africa Regional Update AFRO WHO / UNICEF WCARO</td>
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<tr>
<td>9:30 – 9:45</td>
<td>Region of the Americas Update Jairo Mendez and Alba-Maria Ropero, PAHO</td>
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<tr>
<td>9:45 – 10:30</td>
<td>Brazil Update (15 min presentation MoH, 10 min emerging issues, 15 min discussion) Marcos Boulos, Secretariat of Health, State of Sao Paulo, Brazil</td>
</tr>
<tr>
<td>10:30 – 11:00</td>
<td>Coffee break</td>
</tr>
<tr>
<td>11:00 – 12:00</td>
<td>Perspectives on the evolution of Yellow Fever global risk and</td>
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<td>mechanisms to mitigate this risk Facilitator: Dr. Soce Fall</td>
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<td>Panel: Oyewale Tomori, Pedro Vasconcelos, Marcos Boulos, Erin Staples</td>
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<tr>
<td>12:00 – 12:30</td>
<td>Group photo</td>
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<tr>
<td>12:30 – 14:00</td>
<td>Lunch (Working-lunch for proposed members of Immunization WG)</td>
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<tr>
<td><strong>Session 2: EYE Strategy Implementation Update – Chair: Sylvie Briand (WHO)</strong></td>
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<tr>
<td>Objectives:</td>
<td>- EYE partner update on progress, successes, and current issues (governance, routine immunization (RI)</td>
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<tr>
<td></td>
<td>and vaccine supply, preventive mass vaccination campaigns (PMVC), laboratory and surveillance)</td>
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<td></td>
<td>- Strength partner engagement with clear roles and responsibilities</td>
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<td>- Working group status updates and proposed next steps</td>
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<td></td>
<td>- Provide overview of emerging research and policy issues</td>
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<tr>
<td>14:00 – 14:30</td>
<td>Global update on EYE Strategy Progress (20 min update, 10 min discussion) EYE Secretariat</td>
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<tr>
<td>14:30 – 15:15</td>
<td>Working Group Updates (10 min per group, interactive)</td>
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<tr>
<td></td>
<td>- Risk Analysis &amp; Modeling (Erin Staples)</td>
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<td></td>
<td>- Laboratory (Mick Mulders)</td>
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<td>- Supply &amp; Demand (Heather Deehan)</td>
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<td></td>
<td>- Immunization working group (Kaushik Banerjee)</td>
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<tr>
<td>15:15 – 15:30</td>
<td>Discussion &amp; comment on Working Group</td>
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<tr>
<td>15:30 – 16:00</td>
<td>Coffee break</td>
</tr>
<tr>
<td>16:00 – 17:00</td>
<td>Emerging issues &amp; Research (10 min approx. each, 10 min discussion)</td>
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<tr>
<td></td>
<td>A) Fractional YF Vaccination</td>
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<td></td>
<td>- Fiocruz 8 year study (presenter TBC)</td>
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<td></td>
<td>- Kinshasa 1 year follow up results (presenter TBC)</td>
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<td>B) Co-administration of YF vaccine</td>
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<td></td>
<td>- Update on routine programmes, Erin Staples</td>
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<td></td>
<td>- Combined campaigns, Kaushik Banerjee- Immunization working group (Kaushik Banerjee)</td>
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<tr>
<td>17:00 – 18:30</td>
<td>Cocktail Hour *reminder to sign up for IPD Field Visit</td>
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</table>
## DAY 2 – Wednesday, 12 September 2018

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
<th>Presenter(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:30 – 9:00</td>
<td>Sign-in</td>
<td></td>
</tr>
<tr>
<td>9:00 – 9:15</td>
<td>Re-cap of day 1 and introduction to day 2</td>
<td>EYE Secretariat</td>
</tr>
<tr>
<td>9:15 – 9:45</td>
<td>Global YF Vaccine Roadmap</td>
<td>Michael Clark, Gavi</td>
</tr>
<tr>
<td>9:45 – 10:00</td>
<td>Yellow Fever vaccine procurement mechanisms</td>
<td>Heather Deehan, UNICEF Supply Division</td>
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<tr>
<td>10:00 – 10:15</td>
<td>Discussion</td>
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<tr>
<td>10:15 – 10:45</td>
<td><strong>Coffee break</strong></td>
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<tr>
<td>10:45 – 11:15</td>
<td>Vaccine demand and supply overview for the Americas</td>
<td>Alba Maria Ropero, PAHO (demand) John Fitzsimmons, PAHO Revolving Fund (supply)</td>
</tr>
<tr>
<td>11:15 – 11:30</td>
<td>Discussion</td>
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<tr>
<td>11:30 – 12:30</td>
<td>How can we meet the needs for Yellow Fever vaccine for routine programs and preventive campaigns?</td>
<td>Facilitator: William Perea</td>
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<tr>
<td>12:30 – 13:30</td>
<td><strong>Lunch</strong></td>
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<tr>
<td>14:00 – 14:30</td>
<td>Senegal (15 min presentation, 15 min discussion)</td>
<td>MoH</td>
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<tr>
<td>14:30 – 15:00</td>
<td>Colombia (15 min presentation, 15 min discussion)</td>
<td>MoH</td>
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<tr>
<td>15:00 – 15:15</td>
<td>EYE Country Guidance Toolkit</td>
<td>EYE Secretariat</td>
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<tr>
<td>15:15 – 15:45</td>
<td><strong>Coffee break</strong></td>
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<tr>
<td>15:45 – 16:15</td>
<td>Nigeria Update (10 min presentation, 10 min discussion)</td>
<td>EYE Secretariat</td>
</tr>
<tr>
<td>16:15 – 16:45</td>
<td>DRC (10 min presentation, 10 min discussion)</td>
<td>MoH</td>
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<tr>
<td>16:45 – 17:30</td>
<td>Group Discussion: How can Immunization WG support strengthened routine vaccination coverage?</td>
<td>Facilitator: Kaushik Banerjee</td>
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**DAY 3 – Thursday, 13 September 2018**

<table>
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<tr>
<th>Time</th>
<th>Session Description</th>
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<tbody>
<tr>
<td>8:30 – 9:00</td>
<td>Sign-in</td>
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<tr>
<td><strong>Session 5: Planning Way Forward – Chair: Heather Deehan (UNICEF SD)</strong></td>
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<tr>
<td>9:00 – 9:15</td>
<td>Session intro and re-cap of days 1&amp;2</td>
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<tr>
<td></td>
<td>EYE Secretariat presents:</td>
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<tr>
<td></td>
<td>- progress and lessons learned from 120d plan</td>
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<td></td>
<td>- proposed plans for inclusion in next 180d plan</td>
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<td>defining outputs and proposing responsibilities</td>
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<tr>
<td>10:15 – 10:45</td>
<td>Coffee break</td>
</tr>
<tr>
<td>10:45 – 11:45</td>
<td>B: Global Action plan cont’d</td>
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<td></td>
<td>Partner panel to review and refine outputs and assigning responsibilities</td>
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<tr>
<td>11:45 – 12:15</td>
<td>Recap and summary of next steps</td>
</tr>
<tr>
<td>12:15 – 12:30</td>
<td>Closing remarks</td>
</tr>
<tr>
<td>12:30 – 14:00</td>
<td>Lunch</td>
</tr>
<tr>
<td><strong>Session 6: Institute Pasteur Dakar (IPD) Field Visit</strong></td>
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<tr>
<td>14:00 – 17:00</td>
<td>IPD Laboratory overview and guided tour</td>
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<td>IPD Manufacturing facility overview and tour</td>
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<td></td>
<td>*sign-up in advance on Day1 of meeting required to facilitate visit logistics</td>
</tr>
<tr>
<td></td>
<td>*transport arranged for pick up at King Fahd Hotel</td>
</tr>
</tbody>
</table>
Annex III:
Factsheet on Eliminating Yellow Fever Epidemics by 2026

The Eliminating Yellow fever Epidemics (EYE) strategy is a global and comprehensive long term (2017-2026) strategy targeting the most vulnerable countries and involving many international partners such as UNICEF and Gavi, the Vaccine Alliance. It addresses the global risk by building resilience in urban centres and in areas with outbreak potential, and ensures reliable and sustainable vaccine supply. The strategy consists of three objectives built on lessons learned during recent outbreaks.

**OUR VISION**
A world without yellow fever epidemics.

**OUR MISSION**
Coordinate international action and help at-risk countries to prevent yellow fever outbreaks and to prepare for those which might still occur. We aim to minimize suffering, damage and spread by early and reliable detection and a rapid and appropriate response.

**Key competencies for success**
- Affordable vaccines and sustained vaccine market.
- Strong political commitment at global, regional and country levels.
- High level governance with long-term partnerships.
- Synergies with other health programmes and sectors.
- Research and development for better tools and practices.

Photo credit: WHO/Yoshi Shimizu

World Health Organization

unicef

Gavi
Where risk is high, vaccinate everyone
Reach every child
Risk assessments
Quickly raise population immunity levels through mass vaccination campaigns.
Sustain high yellow fever vaccine coverage in all districts through childhood routine immunization.
Assess the risk of yellow fever epidemics in at risk countries to set priority for interventions.

STRATEGIC OBJECTIVE 2:
Prevent international spread: no exportation
Protect high-risk workers
Apply International Health Regulations (IHR)
Build resilient urban centers
Engage private sector to protect unimmunized workers with sylvatic exposure (eg. oil and mining industry, agro business). Develop innovative approaches to strengthen IHR application in countries at risk or potential for yellow fever. Develop and implement urban readiness plans to enable urban coping with epidemics.

STRATEGIC OBJECTIVE 3:
Contain outbreaks rapidly: no sustained transmission
Detect early
Vaccine supply is ready at all times
Respond immediately
Strengthen surveillance and laboratory capacities. Ensure permanent availability of yellow fever vaccines worldwide for rapid intervention. Launch coordinated control interventions including reactive immunization, community mobilization, vector control and case management.

FOR MORE INFORMATION
www.who.int/csr/disease/yellowfev/en

CONTACT
EYE.Strategy@who.int
Annex IV: Development of the Proposal for Laboratory Capacity and Network Strengthening in Africa for Submission to the Gavi Programme and Policy Committee
MEETING REPORT

Development of the Proposal for Laboratory Capacity and Network Strengthening in Africa for Submission to the Gavi Programme and Policy Committee

Dakar, Senegal
14 September 2018
## Acronyms

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
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<tbody>
<tr>
<td>AFRO</td>
<td>WHO Regional Office for Africa</td>
</tr>
<tr>
<td>CDC</td>
<td>The Centers for Disease Control and Prevention (United States)</td>
</tr>
<tr>
<td>DRC</td>
<td>Democratic Republic of the Congo</td>
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<tr>
<td>ELISA</td>
<td>Enzyme-linked immunosorbent assay</td>
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<tr>
<td>EYE</td>
<td>End Yellow Fever Epidemics</td>
</tr>
<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
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<tr>
<td>Gavi</td>
<td>Gavi, the Vaccine Alliance</td>
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<tr>
<td>IATA</td>
<td>International Air Transport Association</td>
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<tr>
<td>ICG</td>
<td>International Coordinating Group on Vaccine Provision</td>
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<tr>
<td>IgM</td>
<td>Immunoglobulin M</td>
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<tr>
<td>PAHO</td>
<td>Pan American Health Organization</td>
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<tr>
<td>PCR</td>
<td>Polymerase chain reaction</td>
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<tr>
<td>PPC</td>
<td>Programme and Policy Committee</td>
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<tr>
<td>UNICEF</td>
<td>United Nations Children’s Fund</td>
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<tr>
<td>UNICEF SD</td>
<td>United Nations Children’s Fund Supply Division</td>
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<tr>
<td>WHO</td>
<td>World Health Organization</td>
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<tr>
<td>WHO HQ</td>
<td>World Health Organization Headquarters</td>
</tr>
<tr>
<td>YF</td>
<td>Yellow fever</td>
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</tbody>
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Executive summary

A meeting on the development of the proposal for laboratory capacity and network strengthening in Africa was co-hosted by UNICEF and WHO on 14 September 2018 at the King Fahd Palace Hotel in Dakar, Senegal. The event was held back-to-back with the Eliminate Yellow Fever Epidemics (EYE) Strategy Partners’ Meeting, which took place from 11–13 September. The meeting brought together over thirty delegates representing a range of organizations including nongovernmental organizations, programme funders, partners and managers from national laboratories from across the WHO African Region (AFRO).

The proposal, which was submitted to the Gavi Programme and Policy Committee (PPC) in October 2018, calls for 12 million USD of funding to enhance laboratory capacity in the Region. Its scope covers a range of activities, including procurement of reagents, supplies and equipment; technical assistance; quality assurance and quality control; sample transportation; and limited human resources for the period 2018–2020.

The meeting gave delegates the opportunity to share perspectives and contribute any final additions to the funding proposal, which was submitted to Gavi PPC by 21 September 2018. After an overview of the ongoing external assessment of laboratory capacity in the Region, delegates discussed a number of technical issues facing the laboratory network, including cross-reactivity with of current tests with other arboviruses, a lack of clarity on testing algorithms, the ongoing need for external technical assistance and quality assurance, procurement bottlenecks and delays in shipment of samples. Participants agreed on priorities for the EYE Laboratory Working Group going forward as it drafts its work plan for the following 12–18 months.
1. Background: The EYE Strategy

Yellow fever is endemic across Africa and Central and South America, and factors such as climate change, deforestation, urbanization and human population movements have increased risk of transmission in multiple countries. Thirty-five countries in the AFRO Region, home to around 500 million people, are considered to be at risk of yellow fever (YF) outbreaks. Of these, 27 are considered to be at high risk of YF by EYE.

A coalition of the WHO and partner organizations came together in Geneva in September 2016 to devise a new global yellow fever control initiative following two major outbreaks in Angola and the DRC and the threat of a re-emergence of urban YF transmission in Brazil. The EYE Strategy, which aims to tackle the increased risk of yellow fever epidemics in a coordinated manner by 2026, was endorsed by African Ministers of Health at the 67th WHO regional committee in September 2017.

The EYE has three Strategic Objectives:

1. **Protect at-risk populations**
   - Preventive mass vaccination campaigns
   - Vaccinate every child
   - Risk analysis to allocate resources

2. **Prevent the international spread of Yellow Fever**
   - Protect high-risk workers
   - Apply the international health regulations
   - Build resilient urban centres

3. **Contain outbreaks rapidly**
   - Strengthen surveillance and laboratory capacity
   - Ensure availability of emergency vaccine stockpiles
   - Immediate outbreak response

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Currently, the main technical priorities for the Strategy are to:

- Implement preventive mass campaigns in at-risk countries,
- Expand routine immunization,
- Improve laboratory capacity.

Laboratories constitute a key element of the overall EYE Strategy as they are critical for establishing the presence of YF outbreaks. Timely confirmation of cases has the potential to reduce the time between the start of outbreaks and start of emergency response activities. Laboratory confirmation is also essential for applications to the International Coordinating Group (ICG) for Vaccine Provision for release of vaccines from the emergency stockpile. Due to the limited vaccine supply, one major aspect of the EYE Strategy is to prioritize interventions based on risks. Demand for vaccines for mass preventive campaigns and routine immunization is driven by awareness of YF risk as a result of effective risk analysis, surveillance and laboratory networks.

The EYE Laboratory Working Group, one of the EYE Strategy’s four technical working groups, was established in December 2017 to support building powerful yellow fever laboratory capacities in support of the wider EYE Strategy’s activities both at the national and regional levels.

The working group’s priorities are:

- Assessing current capacity at national and regional levels;
- Reviewing laboratory testing protocols;
- Increasing the availability of high-quality diagnostics;
- Improving information sharing between laboratories and with national partners;
- Strengthening quality assurance and quality control; and
- Engaging governments and other partners to advocate for the importance of laboratory capacity and sustainable funding for laboratory and surveillance activities.

Expanding laboratory capacity, particularly in the AFRO Region, has been identified as a major priority area. Currently, only one laboratory in the region has the capability to independently confirm a YF outbreak. In addition, a major challenge for YF surveillance is the non-specific presentation of symptoms and co-circulation of malaria and other flaviviruses. Laboratory confirmation can be hampered by cross-reactivity between YF and other flaviviruses, and the diagnostic tests currently employed at the national level in the AFRO Region have low specificity to distinguish between them.
2. A proposal for laboratory capacity and network strengthening in Africa Table contents

The EYE Laboratory Working Group met on 29 June 2018 in Cascais, Portugal, to initiate the development of a three-year plan of action for laboratory strengthening in Africa, set out a technical vision and define its goals. The proposal was first submitted for initial appraisal to the Gavi Programme and Policy Committee (PPC) in May that year. It included up to 12 million USD, and its scope included procurement of reagents, supplies and equipment; technical assistance; quality control and assurance; sample transportation; and very limited human resources for 2018–2020.

The proposal allows for the possibility of continuing support subsequently on the condition that countries gradually assumed the role of sustaining laboratory capacity over a transition period. The PPC agreed in its May meeting that limitations in yellow fever laboratory capacity are impairing the effective use of yellow fever vaccine. The PPC has acknowledged the importance of current YF laboratory capacity limitations and requested that a detailed plan of action to address them be prepared in time for its October 2018 meeting and the Gavi Board meeting the following month before it could authorize funding.

The proposal seeks to enhance both the capacity (in terms of the number of tests laboratories are able to perform) and capability (in terms of the range of tests offered and the reliability and timeliness of case confirmation) of the network. Priorities include improving procurement mechanisms to reduce the frequency of reagent stock-outs, implementation of standardized external quality assurance and accreditation schemes, and enhancing the quality and appropriate flow of specimens and information.

Indicators against which Gavi can measure success of the proposal’s implementation are likely to include the average time needed to confirm YF cases in high-risk countries, the number of African laboratories able to reliably confirm yellow fever cases, and the introduction and distribution of one or more new validated YF diagnostic tests or test kits. Other criteria could also be added, such as cold chain capacity and progress towards addressing the geographic mismatch between YF risk and laboratory capacity.
The meeting for the Development of the Proposal for Laboratory Capacity and Network Strengthening in Africa took place at the King Fahd Palace Hotel in Dakar on 14 September 2018 immediately following the Strategy Partners’ Meeting on 11–13 September. The meeting’s setting, Senegal, was appropriate given that the country is home to the YF reference laboratory for the AFRO Region—the Pasteur Institute in Dakar. It provided an opportunity for partners to update one another on progress to date, and for each to have a final input on technical issues relating to the proposal and engage with representatives from Gavi before its submission to the PPC.

Over thirty delegates participated, including representatives of the World Health Organization (WHO) headquarters (HQ), the WHO Regional Office for Africa (AFRO), the Pan American Health Organization (PAHO), United Nations Children’s Fund (UNICEF) Supply Division (SD), Gavi, the Vaccine Alliance, the Bill and Melinda Gates Foundation, the Centers for Disease Control and Prevention (CDC), the Robert Koch Institute and the Foundation for Innovative New Diagnostics. Representatives of laboratories from across the African region, including the Pasteur Institute in Dakar, the Uganda Virus Research Institute (UVRI) and the Pasteur Centre in Cameroon (CPC), were also represented in addition to ministries of health from individual countries. The proceedings were expertly guided by technical experts and co-chairs of the EYE strategy Laboratory Working Group, Marion Koopmans and Chantal Reuskens, who participated remotely from Erasmus University in Rotterdam, the Netherlands.

The meeting started with an overview of the current structure and content of the proposal for Gavi funding, a vision for its intended outcomes and scope of activities, and outline of how its activities will integrate with and complement the wider EYE Strategy. This was followed by an overview of the current status of YF laboratory capacity in Africa and presentations on the current and potential availability of different diagnostic tests in the AFRO Region and the preferred YF testing algorithm. In the afternoon, discussions focussed on the topics of provision of technical assistance, quality assurance and quality control assessments for national laboratories and options for improving transportation of clinical samples and procurement of key laboratory supplies. The meeting rounded off with a review process for driving completion of the proposal, and delegates were solicited for final comments ahead of its submission to the Gavi board.
3. Current yellow fever laboratory capacity in Africa

The WHO Global Yellow Fever Laboratory Network comprises more than 40 laboratories in the PAHO and AFRO Regions. Laboratories in the network are organized into three tiers according to the range of diagnostic tests and services offered:

- National or sub-national laboratories (NL): Typically Ministry of Health laboratories or academic laboratories designated by the country (e.g. National Public Health Laboratory, Sierra Leone)

- Regional reference laboratories (RRL): Laboratories designated by WHO to serve as a referral testing centre for YF. They typically service a (cross-border) region, providing confirmation to national laboratories (e.g. Pasteur Institute in Dakar, Senegal)

- Global specialized laboratories (GSL): Serve as referral centres for more specialized YF testing and provide technical support to WHO and other partners to improve YF diagnostic testing through training, supplying reagents and developing new assays (e.g. CDC Fort Collins, USA)

3.1. Plans for expansion of the laboratory network

**National laboratories**

Since 2007 the regional YF laboratory network has expanded from 14 to 31 laboratories, of which 26 are in high-risk Gavi-eligible countries (Table 1). There are currently plans for new national laboratories in Equatorial Guinea (a high-risk country) and São Tomé and Principe (a country with lower potential YF risk).

**Regional reference laboratories**

The AFRO Region is currently served by a single reference laboratory—the Pasteur Institute in Dakar. As part of efforts to increase the availability of advanced diagnostics for YF and capacity for confirmation of outbreaks, the regional reference laboratory
network will be expanded from one laboratory to three. The WHO is in the process of finalizing the nomination of the Uganda Virus Research Institute (UVRI) as a regional reference laboratory for YF by end of 2018 and the Pasteur Centre in Cameroon (CPC) by mid-2019.

The **Uganda Virus Research Institute (UVRI)**, based in Entebbe, already carries out confirmatory testing for YF for other countries in Eastern and Southern Africa. The institute has also given Regional training sessions in 2007, 2012 and 2018, and, since 2016, personnel have provided outbreak support and training on the ground to colleagues in Angola and Nigeria. The institute has identified areas for improvement including the need for additional storage space as its capacity for YF testing expands and for hiring and training additional personnel to carry out a greater volume of work. The laboratory continues to benefit from input of technical expertise from CDC Fort Collins, particularly in terms of improving quality control and assurance, and one staff member received training at CDC Colorado in May 2018 on a new ELISA kit.

The **Pasteur Centre in Cameroon (CPC)** in Yaoundé is the national YF laboratory not just for Cameroon, but also Chad, Equatorial Guinea and São Tomé and Príncipe. Its core team comprises three scientists, two permanent technicians and students undertaking attachments. Several gaps have been identified as it works towards becoming a reference laboratory for Central Africa, including training needs, the irregularity of accreditation exercises, and the absence of proficiency tests. Databases were also identified as an area for improvement, with personnel training in data management and a more reliable internet connection highlighted as specific needs.

The Pasteur Institute in Dakar will remain the centre of excellence for the AFRO Region in its role as WHO Collaborating Centre on arboviruses and viral haemorrhagic fevers. The addition of two regional reference laboratories promises not only to strengthen the network overall, but to relieve the burden on the Pasteur Institute in Dakar, increase the geographical accessibility of laboratories with advanced diagnostic techniques, and reduce time needed to transport samples to a reference laboratory for case confirmation.
### Table 1: List of YF laboratories in high-risk Gavi-eligible countries

<table>
<thead>
<tr>
<th>Country</th>
<th>Name of Laboratory</th>
<th>City</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angola</td>
<td>INSP</td>
<td>Angola</td>
</tr>
<tr>
<td>Benin</td>
<td>Institut National de Santé Publique</td>
<td>Benin</td>
</tr>
<tr>
<td>Burkina Faso</td>
<td>Centre Muraz</td>
<td>Burkina Faso</td>
</tr>
<tr>
<td>Burundi</td>
<td>None</td>
<td>Burundi</td>
</tr>
<tr>
<td>Cameroon</td>
<td>Centre Pasteur du Cameroun</td>
<td>Cameroon</td>
</tr>
<tr>
<td>CAR</td>
<td>Institute Pasteur</td>
<td>CAR</td>
</tr>
<tr>
<td>Chad</td>
<td>LABOHGRN</td>
<td>Chad</td>
</tr>
<tr>
<td>DRC</td>
<td>National Institute for Biomedical Research (INRB)</td>
<td>DRC</td>
</tr>
<tr>
<td>Republic of the Congo</td>
<td>None (Refers to Kinshasha)</td>
<td>Republic of the Congo</td>
</tr>
<tr>
<td>Côte d’Ivoire</td>
<td>Institut Pasteur de Côte d’Ivoire</td>
<td>Côte d’Ivoire</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>Ethiopian Public Health Institute / EPHI, Virology and Rickettsiology Unit</td>
<td>Ethiopia</td>
</tr>
<tr>
<td>The Gambia</td>
<td>National Health Laboratory Services, Royal Victoria Teaching Hospital</td>
<td>The Gambia</td>
</tr>
<tr>
<td>Ghana</td>
<td>National Public Health and Reference Laboratory</td>
<td>Ghana</td>
</tr>
<tr>
<td>Guinea</td>
<td>Centre Hospitalier Universitaire Donka, Projet des Fièvres Hémorragiques en Guinée</td>
<td>Guinea</td>
</tr>
<tr>
<td>Guinea-Bissau</td>
<td>Laboratoire National de Sante publique</td>
<td>Guinea-Bissau</td>
</tr>
<tr>
<td>Kenya</td>
<td>Center for Virus Research, Kenya Medical Research Institute (KEMRI)</td>
<td>Kenya</td>
</tr>
<tr>
<td>Liberia</td>
<td>National reference laboratory, Liberia Institute for Biomedical Research campus</td>
<td>Liberia</td>
</tr>
<tr>
<td>Mali</td>
<td>Institut National de Santé Publique</td>
<td>Mali</td>
</tr>
<tr>
<td>Niger</td>
<td>Niamey National Hospital</td>
<td>Niger</td>
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<tr>
<td>Nigeria</td>
<td>Yusuf Dantsoho Memorial Hospital</td>
<td>Nigeria</td>
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<tr>
<td></td>
<td>Maitama District Hospital</td>
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<tr>
<td></td>
<td>Gombe Specialist Hospital</td>
<td></td>
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<tr>
<td></td>
<td>Central Public Health Laboratory</td>
<td></td>
</tr>
<tr>
<td>Senegal</td>
<td>Institut Pasteur de Dakar</td>
<td>Senegal</td>
</tr>
<tr>
<td>Sierra Leone</td>
<td>National Public Health Laboratory</td>
<td>Sierra Leone</td>
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<tr>
<td>South Sudan</td>
<td>None</td>
<td>South Sudan</td>
</tr>
<tr>
<td>Sudan</td>
<td>National Public Health Laboratory</td>
<td>Sudan</td>
</tr>
<tr>
<td>Togo</td>
<td>Laboratoire de Sérologie, Institut National d’Hygiène</td>
<td>Togo</td>
</tr>
<tr>
<td>Uganda</td>
<td>Uganda Virus Research Institute</td>
<td>Uganda</td>
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</table>
3.2. Assessment of the regional laboratory network

To assess programmatic needs and inform funding priorities, Gavi contracted four external consultants to conduct on-site assessments of YF diagnostic laboratories in the AFRO Region from August to October 2018.

Assessments took place on-site with an inspection of laboratory facilities including equipment, power sources and biosafety cabinets. Record inspections encompassed standard operating procedures, testing algorithms, sample transport and storage, biosafety procedures, record-keeping and databases, training records, sample inventory systems, reporting systems and timeliness of reporting of results, quality assurance, quality control and accreditation documentation. Inspections were followed by interviews with laboratory directors and core personnel on protocols, workflow, training needs, sample processing, and surveillance and reporting systems. Finally, staff took part in an exit briefing, which provided an opportunity to review current capacity, highlight any specific gaps or problems to be addressed, and discuss next steps and future plans. Briefings also sought to determine laboratories’ technical capacity and ability to implement molecular testing in the future and current levels of support from national ministries of health and AFRO Region laboratory coordinators.

As of 14 September 2018, national laboratories in Benin, Burkina Faso, Cameroon, Chad, Côte d’Ivoire, Mali, Senegal and Togo had undergone on-site visits and assessment of their facilities and processes while the UVRI (Uganda) had undergone a desk review without a site visit. By the end of October 2018, laboratories in Gambia, Guinea, Guinea-Bissau, Niger, Nigeria, Ghana, Liberia, Sierra Leone, the Republic of the Congo, CAR, DRC, Ethiopia, Kenya, Sudan and South Sudan will also have been assessed.

It was noted that the laboratories assessed benefitted from dedicated, experienced laboratory staff with strong support from institution directors. Other strengths included sample tracking systems, in-country sample transport, data management and results reporting systems. The large majority of laboratories’ facilities were adequate for the range of tests offered, and equipment was generally well-maintained and clean. The assessment also highlighted the strong coordination between surveillance programme and laboratory activities, and cooperation between laboratories and WHO.

A number of areas for improvement were noted, however. In terms of equipment, long-term maintenance contracts were not common and laboratories often did not have a dedicated budget for repairs. Few laboratories featured biosafety cabinets for sample
processing. Temperature monitoring of incubators, refrigerators and freezers was at times absent. Interruptions in electrical supply were cited as a challenge, and back-up generators were only available for some facilities. Another common issue was inadequate space inside facilities, with rooms and equipment sometimes shared across multiple activities. In some laboratories use of autoclaves was limited and biohazard waste was at times mixed with normal waste.

Laboratories reported frequent stockouts of critical reagents delays, which caused significant delays in testing. The current assay employed in the region comprises 10 separate components sourced both in-house and from a variety of commercial suppliers. Laboratories rely on supply of reagents from WHO and the current reagent ordering system is inefficient and unsystematic.

It was also noted that there was sometimes a lack of clarity on testing protocols. This challenge was compounded by the lack of a standardized, externally-validated YF ELISA test kit. Related to this is the need for up-to-date training on current testing protocols, in addition to the lack of a proficiency testing program and regular accreditation reviews. Laboratories were often understaffed with a high turnover of personnel. Staff often worked beyond contracted hours to confirm YF cases and had multiple testing responsibilities and competing priorities such as measles and rubella testing.

Finally, the review highlighted the lack of funding for timely shipment of samples to the regional reference laboratory for confirmatory testing—resulting in delays in confirmation and reporting of cases.

**Accreditation**

The WHO AFRO Stepwise Laboratory Quality Improvement Process Towards Accreditation (SLIPTA) was established to promote the improvement of public health laboratories in developing countries to achieve ISO 15189 standards. SLIPTA measures and evaluates the progress of laboratory systems towards international accreditation and awards a certificate of recognition. SLIPTA enables laboratories to develop their quality management systems in order to produce timely, reliable and accurate laboratory results.

Several laboratories in the regional network, including six in Central Africa, are in preliminary stages of SLIPTA review. While the Uganda Virus Research Institute is making significant progress towards accreditation, the Pasteur Centre in Cameroon has already achieved SLIPTA and ISO accreditation.
4. Technical issues

Laboratory capacity refers not only to facilities, but also the existence of other physical and organizational infrastructure. This includes infrastructure to facilitate delivery of samples and availability of critical reagents and human resources. The EYE Strategy calls for the strengthening laboratory diagnostic capacity in all aspects, particularly in the AFRO Region where the need is most acute. Current challenges include cross-reactivity of current tests with other arboviruses, a lack of clarity on testing algorithms, the ongoing need for external technical assistance and quality assurance, procurement bottlenecks and delays in shipment of samples.

4.1. Availability of diagnostic tests

One goal of the laboratory capacity strengthening proposal is that all laboratories in the Region should eventually have some capacity for molecular testing. Currently, confirmation of YF cases relies on the IgM immunoglobulin test at the national laboratory level, supplemented by RT-PCR and IgM ELISA provided by the regional reference laboratory. Current diagnostic methods suffer from a number of disadvantages, including low specificity (especially for the IgM immunoglobulin test and IgM ELISA), cross-reactivity with other flaviviruses, and no intratypic differentiation of IgM response induced by vaccination. Standard RT-PCR tests used in the Region cannot be used for case confirmation if clinical samples were collected >5 days after fever onset. This poses challenges where individual countries may have limited surveillance capacity or transport infrastructure. No commercial kit is available for these tests, and laboratories are dependent on assays produced in-house by US CDC or the Pasteur Institute in Dakar.

As part of the effort to develop the funding proposal, and to promote the wide availability of advanced YF assays in the Region, Gavi enlisted the support of FIND to review the yellow fever diagnostic market. The review encompassed availability of current and potential YF tests (including integrated kits), options for procurement mechanisms and mechanisms for quality assurance of diagnostic tests procured with Gavi support. This comprised a review of YF testing products which were either available or in development, followed by written surveys and interviews with a prioritized list of manufacturers. Its objectives were to assess the current and potential market for YF diagnostics, identify incentives for the development of new YF assays, and describe potential regulatory requirements and options. Products included in the review included molecular assays, molecular diagnostic probes for nucleic acid, integrated cartridge systems, advanced ELISAs (for YF-IgG and -IgM) and immunofluorescence assays.
Challenges include the relatively small current market size for IgM YF assays (10,000–20,000 tests/year) and uncertainty regarding the size of the market for molecular tests, paucity of data on current and expected laboratory capacities, and the need to establish new diagnostic algorithms which integrate molecular testing and new technologies as they become available.

Preferred options for product approval were also discussed, and the WHO prequalification pathway was highlighted as the most appropriate as it is less stringent compared with US Food and Drug Administration (FDA) approval and YF tests are primarily for use in lower and middle-income countries.

### 4.2. Preferred testing algorithm

In the AFRO Region, the IgM immunoglobulin test is used in national laboratories to determine the presence of antibodies to the YF virus. If positive, the case is considered presumptive positive and the sample is dispatched immediately to the regional reference laboratory (currently the Pasteur Institute in Dakar) for confirmation. If equivocal, the sample is re-tested and sent to the reference laboratory if the second result is either positive or equivocal. At the reference laboratory, samples from presumptive positive or equivocal cases are tested using RT-PCR for samples collected ≤5 days after fever onset and IgM ELISA for cases collected >7 days after onset. Other samples collected at 5–7 days are tested using both methods. All samples found to be positive for YF using Polymerase Chain Reaction (PCR) are considered confirmed cases, while IgM-positive samples are tested using the Plaque Reduction Neutralization Test (PRNT).

One of the primary near-term objectives of the EYE Laboratory Working Group is to finalize a new common laboratory testing algorithm for the AFRO Region by the end of 2018. Its implementation will take place alongside continuing efforts towards upgrading national and regional laboratories and completing the nomination of two more regional reference laboratories by mid-2019. The Laboratory Working Group will evaluate the potential for the introduction of more advanced diagnostics such as PCR at the national level to overcome the issue of cross-reactivity, and whether commercially-available test kits may present a viable alternative. Testing protocols will need to be adapted over time as new tests are made available.

Not all laboratories are using the most up-to-date protocol, and this has been attributed to the fact that it is faster (two versus three days) and uses smaller quantities of reagents. Personnel may also feel more confident in older protocols and may not have received training on the new protocol.
4.3 Provision of quality assurance and technical assistance

The funding proposal will support quality control and assurance, and provision of technical assistance for laboratories in the network. Currently, there is no routine proficiency testing for yellow fever serologic or molecular diagnostic testing in the AFRO Region and training sessions at the national level are often too infrequent. The proposal includes scope for support of site visits (which currently do not occur on a routine basis), preferably on an annual basis, by regional reference laboratory staff with input from the WHO Regional Office to assess laboratory facilities and operations. Such exercises provide an opportunity to troubleshoot and resolve specific issues. Proficiency testing is a cornerstone of laboratory quality assurance and crucial in facilitating reliable routine diagnostic operations. The proposal will support proficiency panel provision, including necessary travel costs, equipment and testing supplies. Funding will also be available for three workshops, one in the PAHO and two in the AFRO Region, which will adopt a “train the trainers” approach. These will cover diagnostic techniques including conventional YF IgM ELISA, differential diagnostic ELISA and PCR, alongside other topics such as interpretation of results, recording and analysis of data, biosafety, sample storage, quality control, sample storage, sample shipping and communication. These will be targeted at senior laboratory personnel, who are in a position to understand the broader context in which their laboratories operate and who can transfer knowledge to personnel. Going forward, regional reference laboratories will be expected to facilitate annual refresher training to foster consistency in processes between national laboratories, with input from external consultants where necessary. Training will balance on-site with sub-regional delivery and will need to be adapted in light of changes to testing algorithms and the availability of new, more advanced assays. In general, this approach to provision of quality assurance and technical assistance will emphasize the self-sufficiency of the African YF laboratory network, and will draw upon the expertise of external contractors, WHO or CDC only when necessary.

4.4. Options for laboratory supply procurement and sustainable financing

Despite the presence of YF outbreaks, no laboratory testing for YF occurred at the national level in Nigeria in 2016 and 2017 due to stock-outs of key laboratory supplies. Delegates discussed the potential for establishing a centralized procurement system with the support of Gavi, through which laboratories can place orders instead of dealing with multiple suppliers directly. Not only would this simplify purchase of key supplies, but pooling demand across the regional network can also contribute to securing more favorable prices and serve as a market shaping tool. This procurement system should handle both
routine and surge requests, be adaptable as new assays are made available, and focus on test kits or integrated, self-contained tests when available. Gavi support can also be useful for addressing logistical problems such as shipping and distribution of reagents. Delegates discussed the possibility of creating an emergency stockpile of essential reagents, preferably based within the Region, for use during large-scale YF outbreaks in which laboratory surge capacity would be needed to confirm greater numbers of cases.

4.5. Improving sample transportation

The proposal for laboratory network strengthening will include funding for improvements in sample transportation. Effective cold chain infrastructure and timely delivery of samples to national and regional reference laboratories are key to ensuring the integrity of samples and rapid confirmation of cases. This is particularly true for PCR, which requires that samples arrive at the laboratory less than 10 days after they are taken from suspected cases. Delegates noted that a country-by-country approach to identifying transportation options and establishing contracts should be implemented. Most laboratories do not have a dedicated budget for YF sample shipments, and the initial priority of the proposal will be to provide funding for international sample transportation. Other priority areas include International Air Transport Association (IATA) training for laboratory staff to handle packaging, securing a reliable supply of packaging materials, and improving domestic sample transportation. The Pasteur Centre in Cameroon is an example of a laboratory that has made considerable progress in improving sample transportation by ensuring packaging staff are IATA trained, and by opening a laboratory payment account with DHL.
5. Discussion

Strengthening laboratory capacity across the AFRO Region requires a multifaceted approach that also emphasizes not only facilities, but also availability of key supplies, human resources and training needs, and organizational infrastructure. To achieve this sustainable funding is needed across all these areas going forward. Laboratory expansion should be aligned with the needs and activities of the wider EYE Strategy and draw upon its momentum. Another theme to emerge from the meeting was the need to improve and optimize data-sharing mechanisms, including development of a code of conduct to encourage open dialogue among countries, regional reference laboratories, and the Laboratory Working Group.

The meeting highlighted the role of country ownership in realizing laboratory network strengthening. To ensure that improvements are sustained into the future, a transition period will be required after 2020 in which budget lines from country governments or other sources are secured with a view to eventual full self-financing. Gavi will also give clarity on what its funding will provide and delineate country responsibilities. Funding will cover a range of materials and activities, including supplies and equipment for national and regional reference laboratories, technical assistance, quality control and assurance, and sample transportation for Gavi-eligible countries based on their need. There may also be scope for non-Gavi-eligible countries to access these resources, but without recourse to Gavi funding. Gavi emphasized that the funding proposal does not cover basic laboratory infrastructure such as buildings and utilities, case-based surveillance activities, salaries of staff or the development of new tests. Funding for detection of other arboviruses will also be outside its scope, except where detecting them will prevent false positives for YF.

In summary, the meeting highlighted the following key challenges facing the YF laboratory network in Africa, and the key areas in which Gavi funding could improve both the capability and capacity of the laboratory network:

Key challenges include:

- Insufficient infrastructure for sample shipping and processing,
- Inefficient reagent procurement mechanisms,
- Lack of clarity on, and standardization of, YF testing protocols,
- Understaffing, high rate of turnover of personnel, and training needs.
Key areas in which Gavi funding could enhance the capacity of the laboratory network include:

- Bulk procurement of YF MAC-ELISA reagents and supplies,
- Procurement and distribution of validated YF MAC-ELISA test kits,
- Material support (supplies and equipment) for YF molecular testing,
- YF diagnostic laboratory training workshops and QC programs,
- Shipping of samples.
6. Next steps

The Laboratory Working Group agreed on its priorities going forward for enhancing laboratory capacity in the AFRO Region, which would be incorporated into its work plan for 2019–2020. Delegates agreed that the proposal for laboratory capacity and network strengthening, in addition to the activities of the Laboratory Working Group going forward, should incorporate the following priorities:

- The urgent need for improved procurement mechanisms for critical reagents and improved specimen transport;
- The need to establish biobanks at the regional or global level and to accelerate the development of proficiency panels for use in quality control and assurance;
- The importance of refining YF testing algorithms;
- The need to improve data sharing between laboratories and with WHO;
- The demand for ongoing investment to develop and introduce new and improved tests including the MAC ELISA HD and self-contained test kits; and
- The need for a participatory approach with strong representation of three regional reference laboratories in Africa with an emphasis on coordinated external quality control and assurance and provision of training for national laboratories.

In terms of advocacy, the working group, within the wider EYE Strategy, would seek to engage ministries of health and country-level partners in high- and moderate-risk countries in particular to raise awareness of the importance of securing sustainable funding for YF laboratory and surveillance infrastructure and activities in all aspects—preferably from country government sources.
6.1. Timeline of events

September 2018
Finalization of the Plan of Action to be submitted to Gavi PPC by 21 September 2018.

October 2018
Gavi held its PPC meeting in Geneva in October 2018.

December 2018
The Laboratory Working Group will hold a meeting in Rotterdam, Netherlands on 10–11 December with a view to finalizing its combined laboratory testing algorithm for the AFRO Region by the end of the year and drafting its work plan for the following 12–18 months.

End 2018
The assessment of the regional laboratory network and final summary report with recommendations are expected to be complete by the end of 2018.

Mid-2019
The AFRO Region will be home to three YF reference laboratories with the addition of the Uganda Virus Research Institute and the Pasteur Centre in Cameroon alongside the Pasteur Institute in Dakar.
Sub-Annex I: Meeting agenda

Concept note
Development of the proposal for Lab Capacity and Network Strengthening in Africa (EYE-D), for submission to the Gavi PPC
Dakar, Senegal, 14 September, 2018

Background
Yellow fever epidemics are a potential threat to global health security. Twenty-seven countries in Africa and 13 countries in the Americas are at highest risk for YF epidemics. The global strategy to Eliminate Yellow fever Epidemics (EYE) was developed in the aftermath of an unprecedented urban yellow fever outbreak that initiated in Angola and spread to DRC, with 11 cases exported to China, in 2016. It aims at protecting at-risk population, containing outbreaks rapidly, and preventing international spread.

Currently, the main priorities for the Strategy are to:

- implement preventive mass campaigns in at-risk countries;
- expand/introduce routine immunization;
- improve laboratory capacity for diagnosis, and tracking of yellow fever outbreak elimination.

Due to the limited vaccine supply, one of the primary aspects of the EYE Strategy is to prioritize public health interventions based on risks. Given the current limitations on yellow fever diagnosis capacity in Africa, strengthening the yellow fever laboratory network is crucial for rapid detection of cases and outbreak characterization.

The EYE laboratory technical working group was established in December 2017 to support building powerful yellow fever laboratory capacity, both at national and regional levels as part of the EYE Strategy. Additionally, some representatives from the working group were asked to assist in developing a grant proposal for the to be presented to the Gavi Board’s Programme and Policy Committee (PPC) in October 2018 to part of a case for Gavi investment to build yellow fever laboratory capacity. Representatives of the working group and experts from organizations interested in strengthening yellow fever laboratory capacity in support of the EYE strategy met on 29 June in Cascais, Portugal, and on September 14 in Dakar, Senegal, to brainstorm and share ideas as input for this longer term strategic plan.

The October proposal will build on the more general twofold proposal that was put before the PPC in May 2018 by the Gavi Secretariat and addressed diagnostic procurement mechanisms on the one hand and strategies to increase laboratory capacity. This May
The proposal included up to 12 million USD with a scope including procurement of reagents, supplies and equipment; technical assistance; quality assurance/quality control; sample transportation; and very limited human resources for 2018-2020, with the possibility of continuing support afterwards as long as responsibility of supporting laboratory capacity gradually transitioned to the recipient countries. The PPC acknowledged the importance of current yellow fever laboratory capacity limitations and requested a detailed plan of action to address them be prepared in time for its October 2018 meeting and the Gavi Board meeting the following month. Gavi PPC and Board support will allow Gavi’s investment in the global EYE strategy to expand to include strengthening yellow fever diagnostic capacity.

Given the current window of opportunity, this second brainstorm meeting will build upon the work carried out since the event in Cascais, in June 2018, to finalize the laboratory network components of the laboratory capacity investment proposal to be submitted to the Gavi PPC in October.

The 2nd meeting for the EYE-D proposal development will be held on 14 September, in Dakar, Senegal, back-to-back to the EYE Annual Partners Meeting (11-13 Sept.).

Methods of work: The components of the investment proposal dealing specifically with laboratory network functions will be sent to participants prior to this meeting (toward the end of August). Comments and inputs will be expected by e-mail by 05 September. The EYE Secretariat will assemble the comments in an updated proposal that will be finalized during the meeting.

Plenary discussions and group work on the different sections of the document will support refine/finalize the proposal.

Expected outcome: Finalization of the Plan of Action to be submitted to Gavi PPC by September 20, 2018.

Rapporteur: Sol Richardson

Translation services to be provided: French to English, English to French

WebEx Link: To be circulated in advance of meeting
### Draft agenda

**EYE-D Proposal Development**

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
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<tbody>
<tr>
<td>8:00 – 8:30</td>
<td>Registration and welcome coffee</td>
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<tr>
<td>8:30 – 8:45</td>
<td>Welcome and introductions</td>
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<td><strong>Chair: EYE Lab Working Group</strong></td>
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| 8:45 – 9:15| Potential for Gavi support for yellow fever diagnostic laboratory capacity as part of EYE strategy  
- overview of structure and content of proposal  
- vision of outcome and scope of activities  
- how this integrates w- EYE  
- emphasis for the day activities |
| 9:15 – 9:45| Overview of current status of YF laboratory capacity in Africa          |
| 9:45 – 10:15| **Coffee break**                                                        |
| 10:15 – 11:00| Yellow fever diagnostic test current and potential availability       |
| 11:00 – 12:30| Preferred yellow fever testing algorithm  
- emphasis on what is preferred and feasible |
| 12:30 – 13:30| **Lunch**                                                               |
| 13:30 – 15:00| Provision of technical assistance and quality assurance/quality control assessments |
| 15:00 – 15:15| Options for improving sample transportation                            |
| 15:15 – 15:45| **Coffee break**                                                        |
| 15:45 – 16:30| Possible options for laboratory supply procurement and sustainable financing |
| 16:30 – 17:15| Algorithm finalized  
- Algorithm finalization & review                                     |
| 17:15 – 17:30| Next steps  
- Review process for driving completion of proposal  
- Comments / contributions due by COB Tues 18 Sept 2018 |
| 16:45 – 17:00| Closing remarks & Thank-you                                              |
Sub-Annex II: List of participants

WHO

Mick Mulders
GYFLN/Global VPD Laboratory Networks
HQ/IVB

Laurence Cibrelus
HQ/IHM

Kaushik Banerjee
HQ/IVB

Jennifer Horton
HQ/IHM

Annick Dosseh
IST-West

Charles Byabamazima
IST-East and South

Jude Kfutwah
IST-Central

Lab Strengthening Team
WHO Lyon (nomination tbc)

Gavi Secretariat

Lee Hampton
Anais Colombini

Institute Pasteur Dakar

Amadou Sall
Gamou Fall
Ousmane Faye

Uganda Viral Research Institute

Julius Lutwama

Centre Pasteur Cameroon

Maurice Demanou

Nigeria Centre for Disease Control

Nwando Mba

National Institute for Biomedical Research, DRC

Jean-Jacques Muyembe

Erasmus University

Marion Koopmans (via Webex)
Chantal Reusken

US CDC

Jane Basile
Christine Goodman
Christopher J. Gregory
Erin Staples
Eric Mossel

Bill and Melinda Gates Foundation (BMGF)

Tina Lorenson

Robert Koch Institute (RKI)

Cristina Domingo
Mathias Niedrig

FIND

Camille Escadafal

Consultants and others

Barbara Johnson
Herve Zeller