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Background

Yellow fever is endemic in tropical areas of Africa and Central and South America. The disease is spread by Aedes aegypti mosquitoes. WHO is particularly concerned about stopping the spread of yellow fever in urban areas where immunization levels are not sufficient (less than 80% of population has immunity) and where mosquitoes are present in high densities. Overcrowded settings with inadequate water supply and waste management services allow the mosquito to breed easily.

Since January 2016, a number of you have been involved in the yellow fever outbreak response and/or are planning and preparing to contain the spread of the disease across national borders. Vaccinations are the most effective measures for preventing the disease and cognizant of this, we acknowledge that many of us, including our stakeholders, are not aware of how to quickly access the global stockpile of emergency vaccines for yellow fever. The International Coordinating Group for the Provision of Vaccines (ICG) – a partnership comprised of WHO, UNICEF, Médecins sans Frontières (MSF) and the International Federation of the Red Cross and Red Crescent Societies (IFRC) – manages the mechanism and accompanying procedures for securing vaccines when insufficient supplies are available within a country.

In order to facilitate a better understanding of this mechanism and issues surrounding the coordinated distribution of vaccines to areas that are most in need, we are sending you risk communication and community engagement tools developed for your use as well as for distribution to country counterparts.

At page 5 you will find an interactive PDF page containing the guidance and tools on Yellow fever. Click on the icon for the item you wish to read. Any updates will be posted at the same location, so that the interactive PDF remains up-to-date.

Please note that the documents are being translated into official WHO languages, commencing with Portuguese, Spanish and French.

If you have suggestions on how to improve these products or if you would like to provide any other feedback, please write back to us at riskcommunication@who.int
1. **YF basic communication documents:**

**Factsheet on Yellow fever**

- AR
- CH
- EN
- FR
- RU
- SP
- PT

**Q&A on Yellow fever**

- AR
- CH
- EN
- FR
- RU
- SP
- PT

**Q&A on Yellow fever in Angola and Congo**

- AR
- CH
- EN
- FR
- RU
- SP
- PT

2. **Yellow fever vaccine & the ICG**

**Q&A on the International Coordinating Group (ICG) on Vaccine Provision**

This document developed with UNICEF provides basic facts about the ICG mechanism to access vaccine stockpiles during an emergency.

- EN
- PT

**Timeline showing the demands on the global vaccine supply since early 2016**

- EN
- PT

**Video explaining how the global vaccine stockpile works**

English subtitles – soon available with subtitles in Spanish and Portuguese.

- EN
- FR

**Infographic on yellow fever supply in an emergency**

- EN
- PT

**WHO statement on fractional dosing**

- EN
- FR
- PT

3. **RCCE resources and tools**

**Risk communication and community engagement useful links:**

**Yellow Fever Strategic Response Framework June-August 2016**

This document, developed with partners including UNICEF and Médecins Sans Frontières, is intended to guide the international response to the 2016 outbreak.

- EN

**Yellow Fever webpage:**

- EN

**Yellow Fever emergency webpage:**

- EN
- FR

4. **Key response documents and links**

**WHO Secretariat information paper - Fractional dose yellow fever vaccine as a dose-sparing option for outbreak response**

- EN

**Interim technical guidance “Laboratory diagnostic testing in Africa”**

- EN

5. **Additional documents**

**Q&A: Fractional doses of the yellow fever vaccine**

- EN
- FR

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Basic communication documents
WHO Response in Angola and Democratic Republic of the Congo

- WHO is concerned about the yellow fever outbreak in Angola and the Democratic Republic of the Congo (DRC) and has been working closely with the Governments and partners on the outbreak response, including supporting vaccination campaigns, strengthening disease surveillance and providing guidance to improve diagnosis and patient care.
- This is the first time that WHO has activated an Incident Management System for an outbreak response on the ground.
- WHO's Yellow Strategic Response framework identifies 4 objectives to end the outbreak:
  - End current outbreaks through vaccination programs
  - Prevent deaths and illness through early detection and case management
  - Prevent international spread of the disease
  - Prioritize yellow fever vaccine research to improve access
- Vaccination is the key focus of our strategy to control this outbreak.
- WHO has sent more than 18 million doses to Angola, DRC and Uganda, through the International Coordinating Group global stockpile. This is three times the volume normally expected to be needed in one year for outbreak use and is unprecedented. In the past, the global stockpile has never used more than 4 million doses to control a yellow fever outbreak in a country.
- Angola has received 15 million doses, DRC 3.2 million doses, Uganda 800 000 doses.
- WHO has deployed more than 150 experts to support this outbreak and plans to send more teams in the coming weeks.
- A well-planned additional emergency vaccination campaign is imminent to stop ongoing transmission along border areas between Angola and DRC and in the city of Kinshasa.
- An immediate priority is to stop the outbreak in Kinshasa DRC by vaccinating around 10 million people, This campaign is likely to start in August depending on the arrival of vaccine supplies and other logistical issues. Dose fractioning will be used for this campaign as an efficient way to use limited stocks of vaccine to protect the people of Kinshasa before the next rainy season starts.
- A vaccination campaign targeting around 4 million people on border areas between DRC and Angola is likely to use full doses.
- WHO urgently needs $72.35 million to respond to these outbreaks.

Dose fractioning – an “emergency vaccine”

- WHO’s Strategic Advisory Group of Experts (SAGE) on Immunization found that using a fifth of a standard vaccine dose would still provide protection against the disease for at least 12 months and possibly much longer. More studies are needed to determine how long this immunity would last beyond 12 months.
- The SAGE experts said that this method should only be considered in response to an emergency situation in which current vaccine supply is insufficient. It will not be used for routine vaccination or for people who wish to travel.
- This fractional dose will not entitle people to a yellow fever certificate under the IHR. Until further information is available about longevity of the fractionated dose, people will need to have the full dose to entitle them to a certificate.
In any setting where dose fractioning is considered, social mobilization and risk communication will be very important in order to gain health worker and community acceptance and to dispel rumours and misinformation. People will need to be informed that fractional dosing does not mean partial efficacy or an inferior vaccine.

**IHR regulations**

- On 11 July 2016, the policy of lifetime dose of yellow fever vaccine comes into force under the International Health Regulations. This means that all countries must accept a yellow fever vaccination certificate as valid for the life of the person holding it.

- SAGE experts agreed in 2013 that one full dose of yellow fever vaccine is effective in providing immunity for life. A booster vaccination is no longer required.
Key facts

- Yellow fever is an acute viral haemorrhagic disease transmitted by infected mosquitoes. The "yellow" in the name refers to the jaundice that affects some patients.
- Symptoms of yellow fever include fever, headache, jaundice, muscle pain, nausea, vomiting and fatigue.
- A small proportion of patients who contract the virus develop severe symptoms and approximately half of those die within 7 to 10 days.
- The virus is endemic in tropical areas of Africa and Central and South America.
- Since the launch of the Yellow Fever Initiative in 2006, significant progress in combatting the disease has been made in West Africa and more than 105 million people have been vaccinated in mass campaigns. No outbreaks of yellow fever were reported in West Africa during 2015.
- Large epidemics of yellow fever occur when infected people introduce the virus into heavily populated areas with high mosquito density and where most people have little or no immunity, due to lack of vaccination. In these conditions, infected mosquitoes transmit the virus from person to person.
- Yellow fever is prevented by an extremely effective vaccine, which is safe and affordable. A single dose of yellow fever vaccine is sufficient to confer sustained immunity and life-long protection against yellow fever disease and a booster dose of the vaccine is not needed. The vaccine provides effective immunity within 30 days for 99% of persons vaccinated.
- Good supportive treatment in hospitals improves survival rates. There is currently no specific anti-viral drug for yellow fever.

Signs and symptoms

Once contracted, the yellow fever virus incubates in the body for 3 to 6 days. Many people do not experience symptoms, but when these do occur, the most common are fever, muscle pain with prominent backache, headache, loss of appetite, and nausea or vomiting. In most cases, symptoms disappear after 3 to 4 days.

A small percentage of patients, however, enter a second, more toxic phase within 24 hours of recovering from initial symptoms. High fever returns and several body systems are affected, usually the liver and the kidneys. In this phase people are likely to develop jaundice (yellowing of the skin and eyes, hence the name 'yellow fever'), dark urine and abdominal pain with vomiting. Bleeding can occur from the mouth, nose, eyes or stomach. Half of the patients who enter the toxic phase die within 7 - 10 days.

Yellow fever is difficult to diagnose, especially during the early stages. More severe disease can be confused with severe malaria, leptospirosis, viral hepatitis (especially fulminant forms), other haemorrhagic fevers, infection with other flaviviruses (e.g. dengue haemorrhagic fever), and poisoning.

Blood tests (RT-PCR) can sometimes detect the virus in the early stages of the disease. In later stages of the disease, testing to identify antibodies is needed (ELISA and PRNT).

Populations at risk

Forty seven countries in Africa (34) and Central and South America (13) are either endemic for, or have regions that are endemic for, yellow fever. A modelling study based on African data sources estimated the burden of yellow fever during 2013 was 84 000–170 000 severe cases and 29 000–60 000 deaths.

Occasionally travellers who visit yellow fever endemic countries may bring the disease to countries free from yellow fever. In order to prevent such importation of the disease, many countries require proof of vaccination against yellow fever before they will issue a visa, particularly if travellers come from, or have visited yellow fever endemic areas.

In past centuries (17th to 19th), yellow fever was transported to North America and Europe, causing large outbreaks that disrupted economies, development and in some cases decimated populations.
Transmission

The yellow fever virus is an arbovirus of the flavivirus genus and is transmitted by mosquitoes, belonging to the Aedes and Haemogogus species. The different mosquito species live in different habitats - some breed around houses (domestic), others in the jungle (wild), and some in both habitats (semi-domestic). There are 3 types of transmission cycles:

- Sylvatic (or jungle) yellow fever: In tropical rainforests, monkeys, which are the primary reservoir of yellow fever, are bitten by wild mosquitoes which pass the virus on to other monkeys. Occasionally humans working or travelling in the forest are bitten by infected mosquitoes and develop yellow fever.
- Intermediate yellow fever: In this type of transmission, semi-domestic mosquitoes (those that breed both in the wild and around households) infect both monkeys and people. Increased contact between people and infected mosquitoes leads to increased transmission and many separate villages in an area can develop outbreaks at the same time. This is the most common type of outbreak in Africa.
- Urban yellow fever: Large epidemics occur when infected people introduce the virus into heavily populated areas with high mosquito density and where most people have little or no immunity, due to lack of vaccination. In these conditions, infected mosquitoes transmit the virus from person to person.

Treatment

Good and early supportive treatment in hospitals improves survival rates. There is currently no specific anti-viral drug for yellow fever but specific care to treat dehydration, liver and kidney failure, and fever improves outcomes. Associated bacterial infections can be treated with antibiotics.

Prevention

1. Vaccination

Vaccination is the most important means of preventing yellow fever. In high-risk areas where vaccination coverage is low, prompt recognition and control of outbreaks using mass immunization is critical for preventing epidemics. It is important to vaccinate most (80% or more) of the population at risk to prevent transmission in a region with a yellow fever outbreak.

Several vaccination strategies are used to protect against outbreaks: routine infant immunization; mass vaccination campaigns designed to increase coverage in countries at risk; and vaccination of travellers going to yellow fever endemic areas.

The yellow fever vaccine is safe and affordable and a single dose provides life-long protection against yellow fever disease. A booster dose of yellow fever vaccine is not needed.

There have been rare reports of serious side-effects from the yellow fever vaccine. The rates for these severe ‘adverse events following immunization’ (AEFI), when the vaccine provokes an attack on the liver, the kidneys or on the nervous system, leading to hospitalization, are between 0.4 and 0.8 per 100 000 people vaccinated.

The risk is higher for people over 60 years of age and anyone with severe immunodeficiency due to symptomatic HIV/AIDS or other causes, or who have a thymus disorder. People over 60 years of age should be given the vaccine after a careful risk-benefit assessment.

People who are usually excluded from vaccination include:

- infants aged less than 9 months, except during an epidemic when infants aged 6-9 months, in areas where the risk of infection is high, should also receive the vaccine;
- pregnant women – except during a yellow fever outbreak when the risk of infection is high;
- people with severe allergies to egg protein; and
- people with severe immunodeficiency due to symptomatic HIV/AIDS or other causes, or who have a thymus disorder.

In accordance with the International Health Regulations (IHR), countries have the right to require travellers to provide a certificate of yellow fever vaccination. If there are medical grounds for not getting vaccinated, this must be certified by the appropriate authorities. The IHR are a legally binding framework to stop the spread of infectious diseases and other health threats. Requiring the certificate of vaccination from travellers is at the discretion of each State Party, and it is not currently required by all countries.

2. Mosquito control

The risk of yellow fever transmission in urban areas can be reduced by eliminating potential mosquito breeding sites by applying larvicides to water storage containers and other places where standing water collects. Insecticide spraying to kill adult mosquitoes during urban epidemics can help reduce the number of mosquitoes, thus reducing potential sources of yellow fever transmission.
Historically, mosquito control campaigns successfully eliminated Aedes aegypti, the urban yellow fever vector, from most of Central and South America. However, Aedes aegypti has re-colonized urban areas in the region, raising a renewed risk of urban yellow fever. Mosquito control programmes targeting wild mosquitoes in forested areas are not practical for preventing jungle (or sylvatic) yellow fever transmission.

3. Epidemic preparedness and response
Prompt detection of yellow fever and rapid response through emergency vaccination campaigns are essential for controlling outbreaks. However, underreporting is a concern – the true number of cases is estimated to be 10 to 250 times what is now being reported. WHO recommends that every at-risk country have at least one national laboratory where basic yellow fever blood tests can be performed. One laboratory-confirmed case of yellow fever in an unvaccinated population is considered an outbreak. A confirmed case in any context must be fully investigated, particularly in an area where most of the population has been vaccinated. Investigation teams must assess and respond to the outbreak with both emergency measures and longer-term immunization plans.

WHO response
WHO is the Secretariat for the International Coordinating Group for Yellow Fever Vaccine Provision (ICG). The ICG maintains an emergency stockpile of yellow fever vaccines to ensure rapid response to outbreaks in high risk countries. In 2006, the Yellow Fever Initiative was launched to secure global vaccine supply and boost population immunity through vaccination. The Initiative, led by WHO and supported by UNICEF and national governments, has a particular focus on high endemic countries in Africa where the disease is most prominent. Since the Initiative was launched, significant progress has been made in West Africa to bring the disease under control. More than 105 million people have been vaccinated and no yellow fever outbreaks were reported in West Africa during 2015. The Initiative recommends including yellow fever vaccines in routine infant immunizations (starting at age 9 months), implementing mass vaccination campaigns in high-risk areas for all people aged 9 months and older, and maintaining surveillance and outbreak response capacity. Between 2007 and 2016, 14 countries have completed preventive yellow fever vaccination campaigns. The Yellow Fever Initiative is financially supported by the Global Alliance for Vaccines and Immunization (GAVI Alliance), the European Community Humanitarian Office (ECHO), the Central Emergency Response Fund (CERF), ministries of health, and country-level partners.
Where does yellow fever occur?
Yellow fever occurs in 47 endemic countries in Africa in Central and South America. Around 90% of cases reported every year occur in Sub-Saharan Africa. Infected travellers from areas where yellow fever occurs can export cases to countries that are free of yellow fever, but the disease can only spread easily if that country has the mosquito species able to transmit it, specific climatic conditions and the animal reservoir needed to maintain it.

How do you get yellow fever?
The yellow fever virus is transmitted by infected mosquitoes, most commonly from the Aedes species – the same mosquito that spreads the Zika, Chikungunya and Dengue virus. Haemogogus mosquitoes also spread yellow fever and are mostly found in the jungle. Mosquitoes become infected with the virus when they bite an infected human or monkey. The disease cannot be spread by contact from one person to another.
Mosquitoes breed in tropical rainforests, humid, and semi-humid environments, as well as around bodies of still water in and close to human habitations in urban settings. Increased contact between humans and infected mosquitoes, particularly in urban areas where people have not been vaccinated for yellow fever, can create epidemics.
Outbreaks of the disease are of particular concern when they occur in overcrowded settings with inadequate water supply and waste management services that allow the mosquitoes to breed easily.

What are the symptoms?
Once contracted, the yellow fever virus incubates in the body for 3 to 6 days. Symptoms usually present themselves in 2 phases. The first, "acute", phase usually causes fever, muscle pain with prominent backache, headache, shivers, loss of appetite, and nausea or vomiting. Most patients improve and their symptoms disappear after 3 to 4 days.
However, a small percentage of people enter a second, more toxic phase within 24 hours of the initial remission. They will experience high fever, jaundice, and abdominal pain with vomiting and deteriorating kidney function. Bleeding can occur from the mouth, nose, eyes or stomach, with blood appearing in vomit and faeces. Half of the patients who enter the toxic phase die within 10 to 14 days, the rest recover without significant organ damage.

How is it treated?
There is no specific treatment for yellow fever but good supportive treatment of symptoms, such as dehydration, fever and infection, improves survival rates. Associated bacterial infections can be treated with antibiotics. Yellow fever can be prevented by an extremely effective vaccine that is protective for life.

How is it diagnosed?
Yellow fever is difficult to diagnose (especially during the early stages) because its symptoms can be confused with other common diseases such as malaria, dengue, leptospirosis and Zika virus, as well as with poisoning. Doctors or clinicians who see a sick patient may not be able to tell that they have yellow fever from their symptoms alone, especially if they are in an area where many of these diseases are occurring at the same time.
To confirm a suspected diagnosis of yellow fever, laboratory tests need to be done. Blood tests can detect antibodies produced in response to yellow fever, proving that the person has been infected or vaccinated. Several other techniques are used to identify the virus in blood specimens or liver tissue collected after death. These tests require highly trained laboratory staff and specialized equipment and materials.
**How can it be prevented?**

Vaccine is the most important means to combat yellow fever. The yellow fever vaccine is safe and affordable, and a single dose provides life-long immunity against the disease. To prevent outbreaks in affected regions, vaccination coverage must reach at least 80% of the population at risk. Mosquito control can also help to prevent yellow fever, and is vital in situations where vaccination coverage is low or the vaccine is not immediately available. Mosquito control includes eliminating sites where mosquitoes can breed, and killing adult mosquitoes and larvae by using insecticides in areas with high mosquito density. Community involvement through activities such as cleaning household drains and covering water containers where mosquitoes can breed is a very important and effective way to control mosquitoes.

**Is the vaccine effective and safe?**

Vaccination is the single most important measure for preventing yellow fever. The vaccine has been used for many decades and is safe and affordable, providing effective immunity against yellow fever within 10 days for more than 90% of people vaccinated and within 30 days for 99% of people vaccinated. A single dose provides lifelong protection and costs less than US$ 2. Side effects of the yellow fever vaccine are generally mild and may include headaches, muscle aches, and low-grade fevers. There have been rare reports of serious side-effects.

**Who should be vaccinated?**

In countries where yellow fever occurs, WHO strongly recommends routine vaccination for everyone older than 9 months. During an epidemic, when a mass vaccination campaign is underway, the vaccine is given to everyone over the age of 6 months (when the risk of disease is higher than an adverse event from the vaccine). WHO recommends vaccination for all travellers (with few exceptions) visiting areas where there is risk of yellow fever. Travellers, who have medical grounds for not being vaccinated, must have those grounds certified by the appropriate authorities. Many countries require proof of vaccination against yellow fever before they will issue a visa, particularly if travellers come from or have visited a country where yellow fever occurs. Make sure to keep your yellow fever proof of vaccination safe and bring it with you when you travel to another country.

- [Map: Yellow fever vaccination requirements](#)

**Who should not be vaccinated?**

Some people should not be routinely vaccinated, including:

- infants aged less than 9 months (or less than 6 months during an outbreak, where the risk of disease is higher than an adverse event from the vaccine)
- pregnant women (unless during an outbreak)
- people with severe allergies to egg protein; and
- people with severe immunodeficiency

**Am I protected from yellow fever immediately following vaccination?**

In general, it takes 10 to 14 days from the date of vaccination for a person to develop immunity to the yellow fever virus. Additional personal protection measures from mosquitoes are critically important during this 10-14 day period in yellow fever endemic areas. These include wearing protective clothing, sleeping under insecticide treated bed nets even during the day and using recommended repellents. The vaccination certificate for yellow fever is valid from 10 days after administration of the vaccine for recipients.

**Is eradication of yellow fever possible?**

Eradication of yellow fever is not feasible since we are unable to control the virus in the natural animal hosts.

**Who manages the vaccine supply for yellow fever outbreaks?**

In an emergency situation it is often difficult to get enough vaccine doses to protect the entire population at risk due to the limited global vaccine supply. The emergency stockpile is managed by the International Coordinating Group on Vaccine
Provision for Yellow Fever Control which was created in 2001. The role of the ICG is to verify that eligibility criteria are met by countries applying for outbreak support from the stockpile and to decide on the amount of vaccine to be shipped.

- **International Coordinating Group (ICG) on Vaccine Provision**

**Who manages the yellow fever vaccine supply for routine immunization and preventive mass campaign?**

WHO and UNICEF have the oversight role in tracking and supplying yellow fever vaccine for routine immunization. The YF Initiative (YFI) led by WHO and UNICEF coordinates yellow fever control at the global level. The goals of the Initiative are to prevent yellow fever outbreaks and to secure the supply of yellow fever vaccines. The Yellow Fever Initiative monitors the yellow fever activities at global level and identifies priorities in routine immunization, preventive campaigns, and outbreaks, including yellow fever vaccine supply issues.
Q&A: Yellow fever outbreak in Angola and Democratic Republic of the Congo

17 June 2016  *please notice that this document is subjected to updates*

**What is yellow fever?**
The yellow fever virus is transmitted by infected mosquitoes. Most people have no symptoms. Symptoms may include fever, muscle pain, backache, headache, nausea, vomiting, jaundice, and bleeding from the mouth, nose, eyes or stomach. Vaccination is the most effective way to protect from yellow fever.

- More Q&A's on yellow fever

**Why is there a focus on the current outbreak in Angola?**
The ongoing outbreak of yellow fever in Angola (first reported in December 2015) is notable due to its urban nature. There has been extensive local transmission in Luanda, prompting the vaccination of more than 6 million people in the province since February this year. The epidemic has spread to several other major urban settings in the country. Monitoring and prevention of international spread of the virus from Angola to neighbouring countries and beyond is also a key issue. Local transmission, linked to the epidemic in Angola, has been confirmed in the Democratic Republic of the Congo, while China and Kenya have recorded imported cases.

Yellow fever is endemic in Angola, but this is the first outbreak in 28 years. The last outbreak in the country occurred in 1988 with 37 cases and 14 deaths.

**What is WHO doing to respond to the outbreak?**
WHO and partners are working intensely to control the outbreak by supporting large-scale vaccination campaigns in both Angola and Democratic Republic of the Congo. More than 11 million doses of the yellow fever vaccine have been sent to Angola since February this year and more than 2 million to Democratic Republic of the Congo. The campaigns target provinces where local transmission has been confirmed and aims to immunize over 80% of the population in affected districts. Ensuring targeted vaccination makes best use of global vaccine supplies.

In addition to these mass vaccination campaigns, WHO is supporting the governments of Angola and Democratic Republic of the Congo to:
- Strengthen disease surveillance to ensure rapid detection and laboratory confirmation of suspect cases across the country;
- Implement vector control activities;
- Establish and reinforce community-led social mobilization activities.

**What is WHO doing to prevent spread to neighbouring countries and beyond?**
WHO is working with neighbouring countries, such as Namibia, Democratic Republic of the Congo and Zambia to bolster cross border surveillance with Angola to reduce the spread of infection across borders. The Organization supports the strengthening of vector control measures, including through public health education campaigns and larvae control.

WHO has reminded all countries of the need to enforce yellow fever vaccination requirements for travellers to and from Angola to prevent further spread of the disease. The Organization is also urging travellers to areas with yellow fever to ensure they are vaccinated and carry a certificate.

**Is there a shortage of yellow fever vaccine?**
Global supply of yellow fever vaccine is limited and its use needs to be prioritized and targeted to reach those populations at greatest risk. In the current yellow fever outbreak almost 18 million doses of yellow fever vaccine have been distributed in
emergency vaccination campaigns in Angola, Democratic Republic of the Congo, and Uganda. The global yellow fever emergency vaccine stockpile contains 6 million vaccine doses, normally enough for outbreak response in a year. In the light of the current outbreak, shipments of vaccines ordinarily used in routine immunization programmes in other endemic countries have been temporarily prioritized for use in Angola and other affected countries. WHO and partners are also working with pre-qualified manufacturers to increase global vaccine production.

- **Yellow fever global vaccine stockpile in emergencies**

WHO Strategic Advisory Group of Experts (SAGE) on Immunization reviewed existing evidence that demonstrates that using a fifth of a standard vaccine dose would still provide protection against the disease for at least 12 months and possibly much longer. This fractional dosing could be a safe and effective option for mass vaccination campaigns to control urban outbreaks in situations of acute vaccine shortage.

- **Lower doses of yellow fever vaccine could be used in emergencies**

**Is the current outbreak in Uganda linked to Angola?**

In March this year, Uganda gave official notification of an outbreak of yellow fever. The outbreak is not linked to the Angola outbreak. Results of sequencing indicate strong similarities to the virus which caused a yellow fever outbreak in Uganda in 2010.

**Has the pattern of yellow fever in Africa changed?**

In 2006, the ‘Yellow Fever Initiative’ was launched. Led by WHO, and supported by UNICEF and national governments, the Initiative has made significant progress in West Africa to bring the disease under control. More than 105 million people have been vaccinated since its launch, and no yellow fever outbreaks have been reported in West Africa in 2015 or 2016. However, since 2010, the location of yellow fever has shifted from West Africa to central and east Africa where no preventive mass vaccination campaigns have been conducted. The outbreak in Angola emphasizes the need to strengthen risk assessment and mass vaccination in central and east Africa.

The Yellow Fever Initiative, which focuses on highly endemic countries in Africa where the disease is most prominent, recommends including yellow fever vaccines in routine infant immunizations (starting at 9 months of age), implementing mass vaccination campaigns in high-risk areas for all people aged 9 months and older, and maintaining surveillance and outbreak response capacity.

Between 2007 and 2016, 12 countries have completed mass preventive yellow fever vaccination campaigns: Benin, Burkina Faso, Cameroon, Central African Republic, Côte d'Ivoire, Ghana, Guinea, Liberia, Mali, Senegal, Sierra Leone and Togo. Nigeria and Sudan have commenced preventative mass vaccination campaigns in 2013 and 2014 respectively. Both countries are implementing these campaigns in phases. Nigeria is expected to complete the campaign in 2019 and Sudan in 2017.

The Yellow Fever Initiative is financially supported by Gavi the Vaccine Alliance, the European Community Humanitarian Office (ECHO), the Central Emergency Response Fund (CERF), Ministries of Health, and the country-level partners.
Yellow fever vaccine & the ICG
What is the ICG?

The ICG was established in 1997, following major outbreaks of meningitis in Africa, as a mechanism to manage and coordinate the provision of emergency vaccine supplies and antibiotics to countries during major outbreaks. Working closely with vaccine producers, through WHO and UNICEF, and following disease trends, the ICG monitors its vaccine security global stock levels for cholera, meningitis and yellow fever to ensure availability of sufficient supply to respond to disease outbreaks when they occur.

The ICG brings partners together to improve cooperation and coordination of epidemic preparedness and response. The ICG also works on forecasting vaccine stocks, negotiating vaccine prices through its networks or partners, evaluating interventions and standard protocols for managing diseases.

The ICG's mission is to:
- Rapidly deliver vaccines to respond to disease outbreaks;
- Provide equitable vaccine allocation through careful assessment of risk, based on epidemiological and operational criteria;
- Coordinate the use of limited amounts of vaccines and essential medicines;
- Reduce wastage of vaccines and supplies;
- Advocate for readily available, low-cost vaccines and medicines;
- Work with manufacturers through UNICEF and WHO to guarantee the availability of vaccine emergency stock supplies at the global levels;
- Follow standard operating procedures and establish financial mechanisms to purchase emergency vaccine supplies and ensure their sustainability.

Who are ICG's partners?

The ICG is made up of four member agencies:

**International Federation of the Red Cross and Red Crescent Societies (IFRC)** - Has strong country presence for community health promotion, local social and resource mobilization and provides support to states during disasters and epidemics.

**Médecins sans Frontières (MSF)** - An independent, field-based NGO that provides health care to vulnerable populations in emergency settings.

**United Nations Children's Fund (UNICEF)** - Conducts wide scale vaccine procurement and shipment, and provides technical support on campaign planning and implementation in country focusing specially on social mobilization and cold chain.

**World Health Organization (WHO)** - Provides global public health advice and technical support to countries. During outbreaks, WHO focuses on vaccine stockpile management, surveillance, preparedness and response to disease outbreaks. Additional expertise and technical advice is provided on a case-by-case basis from partners including: Agence de Médecine Préventive in Paris, Epicentre in Paris, GAVI the Vaccine Alliance, WHO Collaborating Centres, the US Centers for Disease Control and the European Community Humanitarian Office (ECHO).

Vaccine manufacturers, vaccine equipment providers and financial donor institutions are also engaged in the ICG operations.

Which vaccine stockpiles are available through the ICG?

ICGs have been established to provide access to vaccines for the following diseases:

**Cholera** - Since 2013, the ICG for Cholera manages the global stockpile of oral cholera vaccine which was created as an additional tool to help control cholera epidemics. Since July 2013, the ICG has released more than 5 million doses of oral cholera vaccines to affected countries.
Meningitis - The ICG on Vaccine Provision for Epidemic Meningitis Control was established in January 1997, following major outbreaks of meningitis in Africa. Since then, 59 million doses of vaccines were shipped for emergency response in 20 African countries.

Yellow fever - Since 2001, 90 million doses of yellow fever vaccine have been released and shipped to countries facing outbreaks. With vaccine manufacturers as partners in the ICG, a stockpile of 6 million doses has been reserved for outbreak response since May 2016.

How does the ICG decide to release emergency vaccine stockpiles?
Vaccine security stocks can be accessed by ANY country facing an epidemic ANYWHERE in the world, as long as the country’s request fulfills ICG’s criteria for release of vaccine stocks. As a first step, a country must complete and submit a request to the ICG Secretariat using the standard application form.

The ICG secretariat at WHO then circulates this request to the partners: UNICEF, Médecins Sans Frontières, the International Federation of the Red Cross, and WHO for review and assessment. Additional requests for information are sent back to the country, if needed. Following a rapid consultation and evaluation process, the decision to release vaccines and other supplies is communicated to the requesting country within 48 hours, once all necessary information has been provided. If approved, UNICEF procures vaccines and injection materials and organizes delivery of vaccines to the country, ideally within 7 days. Requests are evaluated taking into account the epidemiological situation, vaccination strategy, pre-existing stocks in the country and operational aspects of the epidemic response.

How does the ICG manage, procure and purchase vaccine supply stocks?
The ICG ensures that contingency stocks of vaccines are available to immediately respond to a disease outbreak. The emergency vaccine stockpiles are held at the manufacturer's storage facilities until their release is decided by the ICG. UNICEF procures and ships vaccines and supplies on behalf of the ICG. IFRC and MSF support the vaccine logistics and roll out of immunization campaigns on the ground.

Who funds the purchase of the vaccines?
Every year countries experiencing outbreaks use the ICG mechanism to rapidly obtain quantities of high quality vaccine supplies at special prices. Two different funding mechanisms are used to ensure emergency stockpiles of the three vaccines (yellow fever, meningitis and cholera) managed by the ICG.

- Gavi, the vaccine alliance, finances ICG's stockpiles of meningitis, yellow fever and cholera vaccines for Gavi eligible countries.
- A revolving fund mechanism was established in 2010 to replenish the costs of vaccines and supplies in order to ensure continuous availability of vaccines to non-Gavi eligible countries before the beginning of the next epidemic season. The funds are managed and used based on consensus of the ICG members. The revolving fund ensures that the vaccine
supplies are sustained should long term funding shortages occur. The revolving fund is supported by a number of donors and international agencies.

**What are the roles and responsibilities of recipient countries of ICG vaccine stockpiles?**

The decision to release vaccine stocks is grounded in evidence-based criteria that includes; epidemiological evidence of an outbreak, laboratory confirmation of pathogen, cold chain storage capacity, the country’s demonstrated capacity to conduct a vaccination campaign and an accompanying plan of action for mass vaccination. A country must submit this information in full, in order for its request for emergency vaccine supplies to be accepted within 48 hours.

Once the request for vaccine supplies has been accepted, a process is put in place to ship the vaccines and supplies. Prior to shipment, the recipient country must demonstrate that there is enough cold chain capacity to receive and store the vaccines and supplies. The recipient country must also ensure that funds are fully available for operational costs of the immunization campaign. Additionally, customs and regulatory approvals must be granted and provided to the ICG prior to the shipment of the vaccines and supplies.
Yellow fever vaccine supply in an emergency

A health worker suspects yellow fever and takes a blood sample for testing.

The blood sample is sent to a laboratory. Lab results confirm yellow fever.

Lab results go to the Ministry of Health who reports yellow fever cases to WHO.

The Ministry of Health requests vaccines from the ICG.

The ICG makes a decision to release vaccines from the stockpile within 48 hours.

A shipment of vaccines arrives in the country within 7 days.

The International Coordinating Group (ICG)*

The ICG is comprised of UNICEF, MSF, IFRC and WHO. It currently manages the yellow fever vaccine stockpile of 6 million doses and approves deployment of vaccines.

In 2016, the yellow fever vaccine stockpile has been replenished 2 times!

UNICEF and WHO request manufacturers to increase production of vaccines.

It takes 12 months to produce new yellow fever vaccines.

4 vaccine manufacturers work around the clock to produce more and more vaccines.

*The ICG manages emergency vaccine stockpiles for cholera, meningitis and yellow fever to ensure availability of sufficient supply when responding to emergencies.
Lower doses of yellow fever vaccine could be used in emergencies

17 June 2016  *please notice that this document is subjected to updates*

The yellow fever vaccine given as one fifth of the regular dose could be used to control an outbreak in case of vaccine shortages. Experts agreed with this proposal at a meeting convened by WHO to consider potential shortages in yellow fever vaccine due to the outbreak in Angola and Democratic Republic of Congo. WHO Strategic Advisory Group of Experts (SAGE) on Immunization reviewed existing evidence that demonstrates that using a fifth of a standard vaccine dose would still provide protection against the disease for at least 12 months and possibly much longer.

**Fractional dosing: a short term measure**

This approach, known as fractional dosing, is under consideration as a short-term measure, in the context of a potential vaccine shortage for use in emergencies. This approach is not proposed for routine immunization, as there is not yet enough data available to show that lower doses would confer the life-long protection provided by a vaccination with one full dose.

"Yellow fever outbreaks in Angola, Democratic Republic of the Congo and Uganda are placing unprecedented demands on vaccine supply for emergency vaccination campaigns to control the spread of the disease," says Jon Abramson, chair of the WHO Strategic Advisory Group of Experts (SAGE) on Immunization.

"Right now we have enough vaccines in the global stockpile to cope with the ongoing outbreaks if there are no further extensions. However, given the wide spread of the disease in Angola and the potential for it to get out of control in the city of Kinshasa, in the Democratic Republic of the Congo, WHO and partners are seriously considering the use of this dose-sparing strategy to prevent transmission through large-scale vaccination campaigns."

**Vaccine shortages in urban outbreaks**

At the request of the Emergency Committee regarding yellow fever convened by WHO's Director-General on 19 May, the WHO secretariat has been exploring options, based on existing evidence, on ways to increase vaccine supply in case of urgent need.
SAGE was asked to review the evidence and options presented by WHO. A formal evaluation and recommendations by SAGE on the use of lower doses of yellow fever vaccine are planned for October 2016.
In the interim, SAGE found that the available evidence is sufficient to determine that fractional dosing of yellow fever vaccine to one fifth of the standard dose (0.1ml instead of 0.5ml) could be a safe and effective option for mass vaccination campaigns to control urban outbreaks in situations of acute vaccine shortage.
More research is needed to find out whether fractional doses would be effective in young children, who may have a weaker immune response to yellow fever vaccine.
Practical issues on administering the reduced doses need further investigation, including obtaining the necessary supply of suitable syringes.

**International Health Regulations require full dose for travellers**

Yellow fever is the only disease specified in the International Health Regulations (IHR) for which countries may require proof of vaccination from travellers as a condition of entry. The IHR were amended in 2014 to indicate that a single dose of the vaccine is sufficient for life-long immunity and therefore extends the validity of vaccination certificates to the life of the person vaccinated. All countries must abide by this new amendment when it enters into force on 11 July 2016.
A yellow fever vaccine given at a fractional dose would not qualify for a yellow fever certificate under the IHR requirements. Travellers will need to obtain the full dose of the vaccine to be eligible for the yellow fever certificate.
Global supply

WHO has prequalified yellow fever vaccines from 4 different vaccine manufacturers which together produce an annual volume of around 80-90 million doses. Prequalification means that vaccines and medicines meet WHO’s high standards of quality, safety and efficacy.

The global stockpile, funded by Gavi, the Vaccine Alliance, has 6 million doses for emergency use per year and this has already been depleted twice since February of this year. To date, WHO and partners have sent around 18 million vaccine doses to Angola, Democratic Republic of the Congo and Uganda for emergency use to control the current outbreaks.

In addition to fractional dosing, WHO’s SAGE group is looking at ways to prevent yellow fever outbreaks on a long-term basis by strengthening mass vaccination catch-up campaigns in conjunction with improving routine childhood immunization in countries with yellow fever.

WHO’s response strategy to the ongoing outbreaks requires coordinated work with partners in five areas: surveillance and risk assessment, vaccination, case management, social mobilization and risk communication and vector control.
Risk communication and community engagement (RCCE) resources & tools
Communication and social mobilization in yellow fever mass vaccination campaigns

10 points from field experience
Communication and social mobilization in yellow fever mass vaccination campaigns

10 points from field experience
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Pandemic and epidemic diseases publications are available online at www.who.int/csr/resources/publications.
Communication and social mobilization in yellow fever mass vaccination campaigns
### Abbreviations and acronyms

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>AEFI</td>
<td>adverse events following immunization</td>
</tr>
<tr>
<td>AIDS</td>
<td>acquired immune deficiency syndrome</td>
</tr>
<tr>
<td>CAR</td>
<td>Central African Republic</td>
</tr>
<tr>
<td>C4D</td>
<td>Communication for Development (model and methodology developed by UNICEF)</td>
</tr>
<tr>
<td>HIV</td>
<td>human immunodeficiency virus</td>
</tr>
<tr>
<td>IEC</td>
<td>information, education and communication</td>
</tr>
<tr>
<td>NGO</td>
<td>nongovernmental organization</td>
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<tr>
<td>SocMob</td>
<td>social mobilization</td>
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<tr>
<td>SMS</td>
<td>short message service</td>
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<td>YF</td>
<td>yellow fever</td>
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Communication and social mobilization in yellow fever mass vaccination campaigns
**Introduction**

In 2006, the Global Alliance for Vaccines and Immunization (GAVI) Board approved the Yellow Fever Investment Case. A group of 12 yellow fever (YF) endemic countries with the highest epidemic risk in Africa were selected for mass preventive vaccination campaigns. As part of this initiative, an innovative strategy for the control of YF outbreaks was implemented in these high-risk countries. The objective was to control YF and reduce the risk of outbreaks by implementing a two-part strategy:

- inclusion of YF vaccine in routine infant immunization programmes for infants 9 months of age; and
- implementation of preventive mass vaccination campaigns to rapidly increase population immunity in high-risk areas and to protect susceptible older age groups.

As of December 2013, at least 88 million people have been vaccinated, with good coverage rates reported in all 12 of the high-risk countries.

Effective communication techniques – in the form of advocacy, social mobilization, and social and behavioral change – are key to a successful mass vaccination campaign. At a minimum, the Yellow Fever Initiative recommended that certain specific activities be included and budgeted for so that a good-quality campaign is conducted:

- distribution of vaccination cards for coverage monitoring;
- surveillance and treatment of adverse effects following immunization (AEFI);
- waste management;
- independent vaccine coverage survey; and
- social mobilization activities, which should focus on conveying
  - that the greatest number of people possible is needed to have good vaccine coverage
  - the people specifically targeted and specifically excluded for the campaign
  - the risks associated with not being vaccinated and with being vaccinated (e.g. AEFI)
  - how to cover areas of most difficult access, where the disease starts every year; and the most vulnerable populations which have very little or no access to health facilities.

It is important the social mobilization methods that are used during a mass campaign take into account the traditional channels and tools in the target area. Important considerations include the traditional way of communicating in rural areas or the language that is used.

The main objective of this document is to provide evidence-based guidance on conducting practical social mobilization and communication for a YF vaccination campaign, either preventive or reactive. Information is also given on the monitoring and evaluation of communication and social mobilization techniques. These 10 points from field experience will be especially useful for district-level planning.

We aim to impart knowledge from the field about using political structures, communication strategies and grass roots communications; sending key messages; dealing with the local media; training mobilizers; conducting a local assessment; and preparing a local plan. This can be used both in local assessments and district planning at a national level, and will help find the correct media mix in these contexts that balances the effective use of printed materials and social networks.
Communication and social mobilization in yellow fever mass vaccination campaigns
1 Building small-scale activities

A country can be divided into regions or states. Usually, a health campaign covers the whole country or a set of regions. The regions may be divided into departments, and the departments further divided into provinces or subprefectures. Finally, the provinces are divided into cantons. A health district may be at the level of a department or a province, depending on the country.

The district health center is the focal point for nurses and health workers to prepare before the campaign starts.

In a mass vaccination campaign, communication and social mobilization activities take place primarily at the district level. Local radio channels and town criers can be important factors in convincing the people of the community to get vaccinated.

To garner support, the vaccination team must communicate, as appropriate, with the chiefs, the traditional authorities and the district managers to ensure that these key figures are united behind the vaccination campaign. Not only does their participation in the vaccination campaign give a positive example, they may also provide or advise on important functions, such as security, or advocate for vaccination in their district meetings.

Each district also has town criers, whose function is to travel throughout the district’s villages shouting the news, doing publicity, and communicating on issues of health, education, taxes, agricultural issues, politics, jobs and so on. Town criers are the world’s oldest way of communicating; they existed in Europe during the Middle Ages (5th to 15th century) and the Renaissance (15th to 17th century), and in the Americas until the start of the 20th century. Field experience has shown that town criers are the most important channel of communication in rural societies that have low income and education. Half of town criers are illiterate or semi-illiterate.

Whereas mobilizers operate at the district and canton level, the town criers work at the village level. The mobilizers use town criers to get the messages to hard-to-reach areas. Town criers can go where the mobilizers cannot go and they can speak the local language. Importantly, they are well known in each village and people believe them.
Communication and social mobilization in yellow fever mass vaccination campaigns
2 Planning advocacy, communication and social mobilization activities

Changing a behaviour requires two steps: (a) creation or modification of the conditions present in the context to facilitate the change (e.g. providing mosquito nets to reduce the exposure to mosquitoes); and (b) communication of messages to the people to change their knowledge, attitudes and behaviours (e.g. implementing an advocacy, communication and social mobilization strategy).

An advocacy, communication and social mobilization strategy is a combination of messages and channels implemented by a specific organizational unit, which targets specific audiences or selected groups. These three different aspects (advocacy, communication and social mobilization), are all forms of communication.

Advocacy

The objective of advocacy activities surrounding a vaccination campaign is to ensure that government officers remain committed to implementing the campaign. Advocacy often focuses on influencing decision-makers through a variety of channels, including meetings between various levels of government and civil society organizations, news coverage, official memoranda of understanding, and other political events.

Programme advocacy targets opinion leaders at the community level on the need for local action. Media advocacy highlights the relevance of the campaign, puts issues on the public agenda, and encourages local media to cover related topics regularly and in a responsible manner, to raise awareness of possible solutions and problems.

Advocacy activities should also be directed at ensuring that national governments remain committed to implementing YF campaigns through a variety of channels, such as meetings with various levels of government and civil society organizations. It is common to plan meetings in the provinces and districts.

All the district managers, communication focal points, religious leaders, relevant non-governmental organizations (NGOs), educational staff, health staff and mobilizers should be invited to the provincial meetings.

All the canton chiefs, priests, imams and religious leaders, NGOs working there, educational staff, health staff, mobilizers, and town criers should go to the district meetings.

These are important meetings for the campaign. Sometimes, for financial reasons, these meetings are not held, but this omission should be avoided. It is crucial that funds are set aside to cover long-distance transportation and water for the guests. The average cost of a district meeting is US$ 50, which covers water and transportation for all attendees. Local and religious leaders may be invited to speak about the YF vaccination campaign.
Some documents that may be helpful to organize and facilitate the meeting include:

- a letter from the Ministry of Health inviting all to support the campaign
- the main messages of the campaign
- how they could participate in the campaign
- frequently asked questions.

**Communication**

Behavior change communication aims to change knowledge, attitudes and practices among various groups of people. The messages should explore the reasons why people do or do not take action on the information they receive, then focus on changing the actual behavior by addressing the causes identified – for example, social norms or personal attitudes.

Communication methods include mass media channels, such as radio, posters, banners, flyers and cellular phones. In many of the YF vaccination campaigns, radios have been the main communication channel. Due to the nature of the countries involved in YF vaccination campaigns, radio – especially local radio – reaches more people than, for example, television. Radio has many formats, such as radio spots (from 20 to 60 seconds), radio microprogrammes (from one to ten minutes), news, health programmes, music, press releases and official communications.

The aim should be to get all the programmes involved in the campaign – the radio spot alone is not enough. Usually local radios commit themselves to produce information about the campaign when you include them in the publicity list – an example of effective synergy.

**Social mobilization**

Social mobilization brings together community members and other stakeholders to strengthen community participation for sustainability and self-reliance. Social mobilization generates dialogue, negotiation and consensus among a range of players, including decision-makers, local media, NGOs, opinion leaders and religious groups.

Social mobilization thus involves local authorities, leaders and social mobilizers. It reaches all members of the community through the traditional channels of the social networks, including via town criers.
### 3 Identifying the district communications focal point

Each department should have a communications focal point, who is a key person in the YF campaign. Remember, a region is divided into departments, so a region could have up to three or four communications focal points, one in each department. These communications focal points are key to the implementation of communication activities. The functions of a focal point include:

- planning communication activities;
- coordinating communication activities in each department, province and district;
- organizing communication committees at the provincial and district level;
- working with local radios to get them to talk about the campaign and inform the population;
- organizing advocacy and sensibilization meetings with the local authorities, religious leaders and opinion leaders;
- mobilizing social networks at the district and village level, including town criers;
- visiting local leaders and using the traditional communication channels;
- overseeing the mobilizers, community relays, members of the committees and town criers; and
- monitoring the process and outcomes of the communication activities, and applying the monitoring tool for community communication.

YF vaccination is only one of the many health campaigns on a district’s agenda. Other campaigns include polio, measles, mosquito nets, HIV/AIDS and prevention. The communications focal point is, therefore, usually very busy with the demanding range of programmes. It is this person’s duty to follow up on all of the communication activities for the health campaigns in the department, which would require them using a private vehicle or public transportation to move around. Therefore, it would be advisable to fund this position, which would normally comprise around one month of activities. An average of US$ 200 for the focal point would be advisable, who will work on the YF campaign at the same time as other campaigns. The focal point will not work for the YF campaign full time, but their networks and contacts are very valuable to the campaign.
4 Defining the main messages and the specific messages

Main messages

In a campaign, it is very important to have a set of main messages. Experience from YF vaccination campaigns in some countries has shown that the following five main messages are most effective and should be communicated:

- There is a YF vaccination campaign.
- The vaccination against YF will be from _____ to _____.
- During the preventive campaign, all children older than 9 months and adults will be vaccinated, except pregnant women.
- Get vaccinated at the nearest health center or vaccination post.
- Vaccination cards and vaccines are free.

Specific or support messages – such as safety, mode of administration, mode of transmission and the vaccination calendar – should be administered through communication channels like radio programmes, theoretical questions and answers, social mobilization, home visits, town criers and/or interpersonal communications.

Specific messages

Campaign participants need a set of complementary information about YF and the vaccination process. Mobilizers need to explain the details of the vaccination campaign to the population when they visit schools, public places or homes. Journalists need to know what YF is, why the campaign is taking place and how the vaccines will be administered. Decision-makers, politicians and religious leaders need to understand the logistics of the campaign and why they are involved in it.

Experience shows that the best way to present this information is as frequently asked questions (please refer to Annex 3). Point number 8 also shows a reduced version of the poster with the five main messages.
Communication and social mobilization in yellow fever mass vaccination campaigns
5 Training mobilizers in social mobilization

Once the focal points, mobilizers and town criers have been recruited, it is necessary to train them to allow the campaign to run smoothly.

For focal points and mobilizers, the most effective training method is to use a training module with guidelines for social mobilization developed for this purpose. Such a module should include the following components:

- objectives of the campaign
- target group(s)
- main messages
- specific messages (as theoretical questions and answers)
- criteria for recruiting mobilizers
- functions of the mobilizers before, during and after the campaign
- sample of the poster
- samples of any other visual materials.

Town criers are best trained using a different method. It is better for the mobilizers to contact them and explain to them their responsibilities in one or two hours, which includes briefings on:

- the campaign objectives
- what YF is, how to prevent it and why vaccinate against it
- the target group that needs to be vaccinated
- the main messages that were developed at central level.

After they are briefed, town criers could decide on how they would express their oral message and agree on a common format. Remember, sometimes mobilizers and town criers are translating the main messages to a region’s specific language.

Recruitment criteria (some recommendations)

Recruiting mobilizers is an important step that requires some consideration. The criteria applied to the recruitment process should be developed keeping in mind the functions of the social mobilizers.
To understand the recruitment criteria for mobilizers, we must think of a different society than what we may be used to. Messages must be expressed in a direct way. Therefore, the successful candidates should be:

- a resident in the locality
- literate
- credible and respectable to the local population
- an upstanding member of the community
- adept in verbal communication
- experienced in field work, and physically and mentally capable of completing the work
- humble, and not see themselves as superior to other members of the community.

Before the campaign, important activities for the mobilizers are to:

- communicate with each of the target villages, cantons and neighborhoods;
- identify key partners and stakeholders to mobilize, including community leaders, religious leaders, teachers and community health workers;
- fix monitoring indicators, define a timeline and responsibilities, and check implementation stages against the timeline;
- conduct advocacy meetings with local leaders;
- communicate with health personnel and school leaders (public and Koranic, where present);
- get input from individuals and groups on how to spread the campaign messages – they can make suggestions for spreading the word, such as announcing the campaign at major meetings and cultural events (traditional festivals, weddings, baptisms, funerals), and sporting events;
- prepare communication materials in advance so that they are distributed on time (some are produced at the central level, like posters, brochures, banners, which must be distributed). They must be displayed in front of health centers or on busy streets. Display the posters in health centers, schools, mosques, churches, markets and other relevant, visible public places;
- prepare a ceremony for the launch of the campaign in all prefectures, subprefectures, health centers and health posts;
- advocate to the local government authorities, to support the mobilization of the population to the vaccination posts;
- spread the word in partnership with associations, NGOs and other community-based organizations, community workers, and religious leaders;
- advertise the campaign in public places using town criers and megaphones;
- identify communication strategies to reach marginalized populations;
- establish a timetable for advocacy, social mobilization and communication activities; and
- estimate the technology requirements for the social mobilization campaign.
During the campaign, the mobilizers need to:

• strengthen the participation of organized community groups (e.g. women’s and youth organizations);

• announce the contribution of different groups and organizations, which encourages continuing support for other national events;

• involve teachers, parents and children. Children are usually very effective in searching for other children who are affected by the campaign;

• inform the public through print media and radio programmes (e.g. provide radio stations with press releases); and

• hold a formal ceremony to launch the campaign.
Communication and social mobilization in yellow fever mass vaccination campaigns
6 Developing a local assessment and a local communications action plan

Local assessment

A local assessment is conducted by using available information to establish where the campaign stands in terms of communications in a specific district and to organize resources. The focal point must do the assessment before the microplanning so they can present this information at the meeting, and so it can be included in the general planning and budget of the campaign.

The following are examples of assessment questions:

- Who are the target groups? For whom do we have a message?
- What are the main messages to be conveyed?
- What are the objectives of the communications and social mobilization campaigns? Usually the objectives are defined in terms of behavioural change. What do we want them to do? What is the key behaviour we want to change? Are there any barriers?
- Who are the key stakeholders and implementers involved in the communication activities? What will be the role and participation of religious leaders?
- What kinds of communicators exist in the district? Focal points? Mobilizers? Town criers? What are the resources we need for the communication activities? How many mobilizers and town criers are needed?
- What is the political structure of the district, the province and the village? This will be a main communication channel. Is it important to have specific activities with local leaders and chiefs?
- How do communities participate in social mobilization? How do the social networks in urban and rural contexts work? Are there some special plans for hard-to-reach populations?
- How many units of each kind of communication pieces would we need (e.g. banners, posters, flyers, merchandising)?
- What are the three most important communications channels? What channels and media are the most efficient ways to address the people and motivate them?
- Are there efficient communications providers who can support us (e.g., community radio, theatre group)?
Local communications action plan

Usually, there are doubts about how to organize a local communications action plan. A local plan must have the following components:

- number of activities
- tasks for each activity
- target group or audience for each activity
- responsible person, organization or partnership for each activity
- outcome of each activity
- timelines for each activity.

Annex 1 provides a clear idea on how to produce a visual local plan and timeline.
Getting the right media mix

Media mix or channels mix is half of the strategy. The other half is the messages, but there are no general rules for this mix. We select a mix of media or channels based on different reasons:

- the characteristics of the channels (e.g. attractiveness, closeness, audiovisual)
- the population that they reach and the resulting impact
- how effective they are at delivering the messages
- the costs
- how frequently they can be used
- attitudes towards the channels
- technical feasibility.

Several learning points on media mix have been taken from experiences in YF vaccination campaigns in Sierra Leone, Guinea, Côte d’Ivoire and the Central African Republic (CAR), which are outlined below.

In countries that are mainly rural, and have very low income and low literacy, the most efficient channel mixes are town crier + radio + short message service (SMS). Other media or channels can act as a support.

SMS has been used to communicate details of vaccination campaigns during the measles campaign in Uganda, the polio campaign in Angola and the YF campaign in Guinea. In this most recent campaign, 2 million cellular telephones were reached. Some of these SMSs were sent at no cost due to the cooperation of Orange Company (1 200 000 telephones), whereas the rest were sent at low cost with help from Sotelgui Company (800 000 telephones). The target group comprised 6 million people, so when the users received the SMS, they relayed the message to other members of their families and friends, so that the campaign information reached a much wider group, including people without a cellular phone. Of course, SMS is only one component of the formula, but it is becoming a very important component. In many countries, cellular phones were developed before the national landline networks attained mid-level development. Therefore, the main phone is the cellular phone, with all the communicational advantages that it provides.

It is often necessary to allocate funds to ensure that SMS communication can be used, and doing so will allow 2–3 messages to be sent per week. Of course, the impact depends on the reach of the network and how the users employ the telephone, and the cost depends on local factors. The Ministry of Health sometimes has the capability to demand free transmission of SMS messages, but other times companies do the minimum to support government demands. Reserving money to pay for SMS messages can ensure more than one wave of messages. In CAR, the SMS messages reached around 600 000 telephones at no cost. All of the health campaigns in Chad include a SMS component.

Audio messages, recorded in local languages, may make up another important component of the communication campaign, a lesson learned during a campaign in Chad. Illiterate or barely literate people had cellular phones in rural areas. An SMS in French would not be understood by these people, but a short audio message in the local language allows it to be communicated as though the town crier had reached cellular phones.
Radio could be very flexible in broadcasting theoretical questions and answers during different stages of the campaign, such as:

- the definition of the vaccination and the five basic messages (see Section 4), plus messages such as “the last dates to vaccinate are …” and “use this opportunity to …”;
- secondary support messages (e.g. safety of the vaccine, mode of administration and why the vaccination campaign is happening);
- “target” messages, reinforcing the main message;
- why there is a mass YF vaccination, which can be incorporated into interviews, the news or microprogrammes; and
- messages about adverse events following immunization – for example:
  - in a few rare cases, adverse reactions may occur
  - most of the adverse reactions are harmless (benign), and may include fever, headaches, muscle pain, joint pain and itchiness
  - occasionally, there are severe allergic reactions, but they are rare (1 case for every 100,000 vaccines administered) and their onset occurs within minutes of immunization. Patients are advised to remain at the place of vaccination for at least 15 minutes after the administration of the vaccine, and the vaccinator is equipped to manage any such reactions
  - most benign adverse reactions can be treated at the nearest health center. A mechanism for investigating and treating suspected cases of severe adverse reactions has been set up in referral hospitals, regional and district hospitals, and in health centers.

Radio spots and microprogramme messages need to be short and straightforward to promote behaviour change. Instead of trying to explain the symptoms of YF, discuss all the arguments in favor of the campaign using radio panel programmes, social mobilization, interpersonal communication, news programmes and so on. The principle is simple: use short formats for key messages and long formats for supporting messages.

Do not use megaphones unless you have to, and do not use audio buses or t-shirts. Audio buses have been used by political groups as social mobilization channels, but they are noisy and unclear, and did not work well for vaccination campaigns. The megaphones are a waste of money in a society where valuables disappear very fast and become used in other unrelated activities, such as propaganda, parties and marriages. This publication refers to campaigns based on health centers and vaccinations posts. T-shirts are better for polio home-based campaigns, and are used to identify the person who visits the houses. Aprons are more adequate for this kind of campaign and could be reused for the next campaigns.

Equally important as production is materials distribution. It is important to make a distribution plan based on the population that needs to be reached and their geographical location, and to follow up its implementation in a specific timeframe. Ensure distribution of materials from district to the subdistrict. A campaign shows good distribution when all the districts and villages have materials.
SMS sent in the Central African Republic during a yellow fever vaccination campaign:
“From 19 to 25 July 2010 get your free yellow fever shot at the health center, excluding pregnant women and children under 9 months old. UNICEF”.
Communication and social mobilization in yellow fever mass vaccination campaigns
8 Using banners, posters and radio

Banners can be used as signals – for example, in the health centers where vaccination posts are located. Banners can also be used as informational tools; they could be placed on the main road of the district, to spread the word about the vaccination campaign, as shown below in an example from Cote D’Ivoire.

**Vaccination campaign against Yellow Fever**

*It is free!*

**From December 10 to 17, 2010**

*It is free!*

Go to the closest Health Centre or vaccination post

All children over 9 months and adults will be vaccinated, except pregnant women

Posters, meanwhile, can be used as informational and motivational tools. They can be pasted in schools, mosques, churches, health centers, markets, shops and other public places. Usually, a poster shows the basic five messages (see Section 4) and invites people to get vaccinated, as in the below example from Sierra Leone. Posters can also be used as a signalization tool (e.g. posted on a tree behind the rural vaccination post).
For communication by radio, it is often best to provide the scripts to the radio stations at the regional level. Local radios have their own recording resources, their own voices and their own language style. They will produce their own versions in local languages. Only national radio will do some kind of standardization in English or French.

It is very important to respect the local radios, for they are opinion-leaders in their regions. If national standardized scripts are used, it is important that the language is appropriate. It is usually more cost-effective to produce a local version. The most effective approach has been found to be a regional campaign using local radios, and a mix of radio spots, microprogrammes and press releases. The microprogrammes could be useful for the local health authorities and leaders to show their support for the campaign. Local radio costs much less than national radio. The synergy between the two will impact not only the population, but the chiefs, religious leaders and decision-makers.

Annex 2 contains an example of radio transcript from Cote d’Ivoire.
9 Working with networks

Advocacy in social networks

Tips for advocating in social networks:

- Social networks are considered the main communication channel in many countries, but there is not much research about their structures. Therefore, it is necessary to assess social, political and religious networks in these countries.
- Despite how well social networks are working during a campaign, it is necessary to monitor the process.
- Get commitments from schools and the Ministry of Education. Keep schools involved in spreading immunization messages. Promote the dissemination of messages through teachers. Schools are ideal in reaching the target group.
- Involve schools and plan according to school hours. Crowds of young people and danger for children can be avoided if the campaign is done in line with school hours. The mobile posts should dedicate a certain amount of time to each school; in this way, thousands of children and young people can be vaccinated. It is cost-effective, as a large group of people can be vaccinated in a short amount of time. This channel has been used to good effect in Sierra Leone.
- Improve the sensitization of women and youth social groups as socially organized groups.
- One of the first products prepared for CAR was a training module for mobilizers based on the experiences of other YF vaccination campaigns. The Ministry of Health produced their own training module, called Mobilizers guide. Unfortunately, this module was a generic adaptation of their usual training module and did not communicate the correct package of basic messages. Not enough guides were produced, which meant that some mobilizers did not have any written instructions or advice. This was an important mistake, as the failure to deliver a module that was well resourced and specific to the campaign undermined the investment.
- It is important to continue outreach and sensitization activities into the hard-to-reach areas, to ensure that vulnerable populations are reached.

Advocacy with the political networks

Suggestions for advocating in political networks include:

- Sensitization must be directed at local authorities and councils, as these are important groups. There is a tendency to misunderstand these local advocacy meetings at different administrative levels.
- As well as sensitization, it is important for the authorities to be vaccinated themselves during the campaign. When people see leaders getting vaccinated, it reduces the risk of resistance or rumours about the quality of the vaccine.
- Regional advocacy meetings alone are not enough, for there are prefectures and cantons before you reach the village level, where the town criers should be found. They are the main communication channels in rural and low-literacy areas. This is the way information and commands spread in these societies; radios alone are not sufficient.


**Advocacy with religious leaders**

Tips for advocating with religious leaders are:

- Religious and cultural leaders should also be specifically targeted for sensitization through meetings and workshops. Muslim populations in many countries have been very receptive to the campaign messages thanks to this kind of advocacy.

- The Ministry of Health should be involved in this aspect of the campaign by issuing a communication to the religious leaders, showing the importance of the campaign and advocating for the involvement of their followers.

- If it is possible, religious leaders should be encouraged to talk about the campaign during religious services, on the radio and on television.

- Three channels that have been shown to work in a synergistic way are messages from priests and pastors, posters in churches, and mobilizers in churches, referring people to the vaccination posts.

- Usually Fridays and Sundays are religious days for Muslims and Christians. The campaigns should use this opportunity to establish vaccination centers in mosques and churches. A radio message stating that the vaccination will be held in the main mosques and churches would help the outreach of vaccinators and mobilizers.

Annex 3 provides specific messages in a frequently asked question format.
10 Monitoring and evaluating the social mobilization campaign

Monitoring and evaluation is an important part of the social mobilization campaign. The following table provides an example from Sierra Leone on how activities were monitored at district level.

Checklist of activities at district level

<table>
<thead>
<tr>
<th>Activity</th>
<th>District 1</th>
<th>District 2</th>
<th>District 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Translate information, education and communication materials/messages into local languages</td>
<td>Well done</td>
<td>Well done</td>
<td>Well done</td>
</tr>
<tr>
<td>At local radio</td>
<td>At local radio</td>
<td>Radio</td>
<td></td>
</tr>
<tr>
<td>Distribute IEC materials from the district to the subdistricts</td>
<td>Well done</td>
<td>Well done</td>
<td>Well done</td>
</tr>
<tr>
<td>Posters and brochures</td>
<td>Posters and brochures</td>
<td>Posters and brochures</td>
<td></td>
</tr>
<tr>
<td>Sensitize religious/cultural leaders in meetings and workshops</td>
<td>Done</td>
<td>Done</td>
<td>Well done</td>
</tr>
<tr>
<td>Sensitize health subdistrict staff in meetings and workshops</td>
<td>Done</td>
<td>Well done</td>
<td>Well done</td>
</tr>
<tr>
<td>Sensitize councils</td>
<td>Done</td>
<td>Well done</td>
<td>Well done</td>
</tr>
<tr>
<td>Sensitize women and youth social groups</td>
<td>Done</td>
<td>Well done</td>
<td>Well done</td>
</tr>
<tr>
<td>Involve schools, disseminating immunization messages, and disseminate messages by teachers</td>
<td>Done</td>
<td>Done</td>
<td>Done</td>
</tr>
<tr>
<td>Organize outreach</td>
<td>Well done</td>
<td>Well done</td>
<td>Well done</td>
</tr>
<tr>
<td>Hold orientation workshops for health care workers to promote interpersonal communications</td>
<td>Not done</td>
<td>Not done</td>
<td>Not done</td>
</tr>
<tr>
<td>Conduct film show in every subcounty</td>
<td>Not done</td>
<td>Not done</td>
<td>Not done</td>
</tr>
</tbody>
</table>

IEC, information, education and communication.

Based on communication for development (C4D) templates, CAR developed a social mobilization monitoring tool to evaluate the effectiveness of social mobilization at the community level. The tool includes a methodological approach, a sample and a Microsoft Excel database. This database was used to enter the sample data. It included formulas that produced a set of automatic charts that contained basic information.

Annex 4 is a sample form that can be used to monitor social mobilization.
Communication and social mobilization in yellow fever mass vaccination campaigns
## Annex 1  Example of an action plan at the local level

<table>
<thead>
<tr>
<th>No.</th>
<th>Activity</th>
<th>Tasks</th>
<th>Target group</th>
<th>Responsibility</th>
<th>Output</th>
<th>Time schedule</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>Define the communication responsibilities for each community</td>
<td>Select Recruit</td>
<td>Mobilizers</td>
<td>Focal point</td>
<td>IEC responsible by districts and villages</td>
<td>×</td>
</tr>
<tr>
<td>2</td>
<td>Explain the message to disseminate to all of the mobilizers and town criers</td>
<td>Define main messages Produce print copies and distribute</td>
<td>Mobilizers and town criers</td>
<td>Focal point</td>
<td>Messages known and agreed to</td>
<td>×</td>
</tr>
<tr>
<td>3</td>
<td>Social mobilization at district level</td>
<td>Organize meetings</td>
<td>Communities</td>
<td>Mobilizers</td>
<td>Message transmitted to the population</td>
<td>× × × ×</td>
</tr>
<tr>
<td>4</td>
<td>Involve local authorities in the organization of the campaign</td>
<td>Have IEC meetings</td>
<td>Local authorities</td>
<td>Regional authorities</td>
<td>Political support and active participation of the authorities</td>
<td>×</td>
</tr>
<tr>
<td>5</td>
<td>Involve traditional chiefs and religious leaders</td>
<td>Make contacts</td>
<td>Traditional chiefs and religious leaders</td>
<td>Focal point</td>
<td>Participation of traditional chiefs Advocacy from religious leaders</td>
<td>× × × ×</td>
</tr>
<tr>
<td>6</td>
<td>Brief local media and channels</td>
<td>Identify local radios and channels Provide them with scripts and information workshops</td>
<td>Local radio, theatre groups, social organizations</td>
<td>Mobilizers</td>
<td>Focal point</td>
<td>Messages disseminated through local media, channels and organizations</td>
</tr>
<tr>
<td>7</td>
<td>Town criers</td>
<td>Calculate how many town criers will be needed Recruit them Provide them with information and support Confirm the message to be transmitted</td>
<td>Communities</td>
<td>Local IEC committees</td>
<td>Communities will be informed about when and where to go to get vaccinated</td>
<td>× × ×</td>
</tr>
<tr>
<td>8</td>
<td>Batteries for megaphones</td>
<td>Calculate the needs Enter them into the micro planning Fill the megaphones Distribute them in a strategic way</td>
<td>Mobilizers</td>
<td>Focal point</td>
<td>Town criers and mobilizers with functional megaphones</td>
<td>× × × ×</td>
</tr>
<tr>
<td>9</td>
<td>Banners</td>
<td>Plan the quantity of banners necessary for the district Put them at the entrance of the district and in front of health centers</td>
<td>Communities</td>
<td>Mobilizers</td>
<td>Population will be informed about the date and the target group of the vaccination</td>
<td>× × × ×</td>
</tr>
<tr>
<td>10</td>
<td>Disseminate information in national languages at local radios</td>
<td>Identify the radios Get the scripts translated into the local languages Disseminate</td>
<td>Local communities</td>
<td>Focal point</td>
<td>Mobilizers</td>
<td>Population will be informed about the campaign</td>
</tr>
<tr>
<td>11</td>
<td>Distribution of posters, flyers and other print materials</td>
<td>Paste posters Distribute flyers</td>
<td>Population</td>
<td>Mobilizers</td>
<td>Population will be informed about the campaign</td>
<td>× × × ×</td>
</tr>
</tbody>
</table>

IEC, information, education and communication.
Annex 2  Example of radio transcript from Cote d’Ivoire

| Sensibilization radio spot for the health care districts |  |
|---|---|---|
| **Characters** | **Text** | **Effects** | **Observations** |
| Jingle |  | Jingle standard vaccination |  |
| Town crier | Hey hey hey! Pay attention to the news! | Jingle on second level |  |
| Woman | What news? | Jingle on second level |  |
| Town crier | There is a big free vaccination campaign against yellow fever in 31 districts of Cote d’Ivoire from Friday 3rd to Thursday 9th December, 2010. | Jingle on second level |  |
| Woman | Ah ok! It is free! Who will be vaccinated? Where is the vaccination taking place? |  |  |
| Town crier | All children over 9 months and adults will be vaccinated, except pregnant women. Go get vaccinated at the nearest health center or vaccination post. | Jingle on second level |  |
| Nurse | Yellow fever is a viral disease. It is transmitted by a mosquito bite. It manifests itself by fever, headaches, muscle pain, fatigue, nausea and vomiting. Complications develop in 15% of infected persons; these complications are jaundice, abdominal pain, bleeding and kidney involvement. Half of those who develop these complications die. There is no treatment for yellow fever. Immunization is the best form of protection from yellow fever. Immunized persons are protected for at least 10 years. | Jingle on second level |  |
| Man (head of the family) | Madame!! Why do they provide a yellow card to those who have been vaccinated? | Jingle on second level |  |
| Nurse | Yellow cards are free and they act as proof that you are vaccinated. Keep your yellow card in a safe place and produce it when requested, in health centers, schools or for travel. | Jingle on second level |  |
| Man + woman + nurse + plus other family members | Together we will defeat yellow fever. | Jingle on second level |  |
| Jingle up |  | Jingle standard vaccination |  |
Annex 3 Specific messages for yellow fever

Fact sheet: frequently asked questions

1. What is yellow fever?

Yellow fever (YF) is a viral disease. It is transmitted by a mosquito bite. Its symptoms include fever, headaches, muscle pain, fatigue, nausea and vomiting. Complications develop in 15% of infected persons; these complications are jaundice, abdominal pain, bleeding and kidney damage. Half of those who develop complications die. There is no treatment for YF. Immunization is the best form of protection from YF.

2. What type of illness does yellow fever cause?

Illness ranges in severity from fever to severe hepatitis and hemorrhages. Most YF infections show moderate symptoms, but the disease can cause severe, life-threatening illness.

Symptoms of severe infection are brown/red urine; in children, the disease mimics septicaemia.

3. Why organize an immunization campaign against yellow fever?

“N” cases of yellow fever have been registered in the communities of _____ and _____. To prevent epidemics in the country, from __ to __ of _____, the government is organizing, in collaboration with its development partners, a YF immunization campaign in “N” health districts in which there is a high risk of an epidemic.

4. Who will be vaccinated?

Everyone over nine months old.

5. Is the vaccine effective?

Yes. The YF vaccine is very effective. It provides protection against the disease after one week, and immunized persons are protected for life.

6. Is it possible to have the whole family vaccinated?

Yes. You must vaccinate all the members of your family who are over nine months old.

7. Who should not receive the yellow fever vaccine?

There are two groups of people who should not receive the vaccine unless the risk of YF disease exceeds the risk associated with the vaccine:

- infants under 9 months of age.
- pregnant women.

8. Should people with HIV infection receive the yellow fever vaccine?

People with asymptomatic HIV infection may be vaccinated. Only people with an immunodepressed condition associated with HIV and AIDS will not be vaccinated.
9. **Is it possible for a malaria patient to be vaccinated?**
   Yes. Malaria is not a contraindication for the vaccine.

10. **Are adverse reactions to be expected?**
    The YF vaccine is very well tolerated. In a few rare cases, adverse reactions may occur.

11. **What kind of adverse reactions are possible?**
    Most of the adverse reactions are benign. They include fever, headaches, muscle pain, joint pain and itchiness.

12. **Are severe allergic reactions possible?**
    Yes, but such reactions are the exception (1 case for every 100 000 doses of vaccine administered) and their onset occurs within minutes of immunization. Patients are advised to remain at the place of vaccination for at least 15 minutes after administration of the vaccine. The vaccinator is equipped to manage any such reactions.

13. **What should be done in case of adverse reactions?**
    It is possible to treat most benign adverse reactions at the nearest health center.

    A mechanism for investigating and treating suspected cases of serious adverse reactions has been set up in referral hospitals, regional and district hospitals, and in health centers.

14. **Where will immunization take place?**
    In the health centers and at a number of temporary immunization posts set up in schools, and at markets, bus stations, churches and neighbourhoods in each of the ____ districts concerned by the immunization campaign.

15. **What happens if a parent fails to bring their children or relatives for immunization?**
    The benefits of immunization should be explained to the parent, and their misconceptions dispelled.

16. **What role does the community play in this campaign?**
    Follow the instruction to come with your family to the YF vaccination posts from the ____ to the ____.

    The community provides information on the campaign, identifies immunization sites, directs people to the sites, and monitors and declares any adverse events.

17. **As a citizen, what part am I able to play to ensure the success of this campaign?**
    Inform those around you about the campaign, identify immunization sites and get yourself, and your family, neighbours and friends vaccinated.

**A message from the Ministry of Health.**
## Annex 4  Sample form to monitor social mobilization

<table>
<thead>
<tr>
<th>Questionnaire code:</th>
<th>Subprefecture:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before □ During □ After □</td>
<td>Community:</td>
</tr>
<tr>
<td>Region:</td>
<td>Neighbourhood/village:</td>
</tr>
<tr>
<td>Prefecture:</td>
<td>Urban □ Rural □</td>
</tr>
</tbody>
</table>

1. Will you vaccinate your family against yellow fever next week?  
   - Y □ □ □ □ □ □ □ □ □  
   - N □ □ □ □ □ □ □ □ □  

2. Did you vaccinate your family against yellow fever this week?  
   - Y □ □ □ □ □ □ □ □ □  
   - N □ □ □ □ □ □ □ □ □  

3. Have you received information about this yellow fever campaign?  
   - Y □ □ □ □ □ □ □ □ □  
   - N □ □ □ □ □ □ □ □ □  

4. If yes, how have you received the information?  
   - Radio? □ □ □ □ □ □ □ □ □  
   - Television? □ □ □ □ □ □ □ □ □  
   - Newspaper? □ □ □ □ □ □ □ □ □  
   - Poster, banner, flyer? □ □ □ □ □ □ □ □ □  
   - Town criers? □ □ □ □ □ □ □ □ □  
   - Churches/mosques? □ □ □ □ □ □ □ □ □  
   - Neighbours? □ □ □ □ □ □ □ □ □  
   - Social mobilizers? □ □ □ □ □ □ □ □ □  
   - SMS? □ □ □ □ □ □ □ □ □  
   - Others? What? □ □ □ □ □ □ □ □ □  

5. Do you know what disease they are vaccinating against in this campaign?  
   - Y (if they say yellow fever) or N (if they say something else) □ □ □ □ □ □ □ □ □  

6. How long will the vaccine protect one against yellow fever?  
   - Y (if they say for life) N (if they say something different) □ □ □ □ □ □ □ □ □  

7. Did you know the mobilizer or the town crier who came to your home?  
   - Y or N □ □ □ □ □ □ □ □ □  

8. Did the mobilizer or the town crier have good behaviour?  
   - Y or N □ □ □ □ □ □ □ □ □  

Note: Y for yes and N for no.
Communication and social mobilization in yellow fever mass vaccination campaigns
Risk Communication and Community Engagement (RCCE) Guide

Yellow Fever Outbreak 2016
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Introduction

Objectives and target audience
This document aims to outline key considerations, strategies and key actions for effective risk communication and community engagement (RCCE) for responding to the 2016 yellow fever (YF) outbreak in Africa. It was initiated by WHO and had substantive inputs from key operational partners UNICEF and IFRC. It is intended to be a resource for stakeholders including, but not limited to, the following:

1. Incident managers and other team leads at the country level (in countries that are currently affected as well as those at-risk) involved in the yellow fever response (or readiness) to help them easily scope out major RCCE issues, strategies, behaviours and messages
2. Risk communication, community engagement, health promotion, social mobilization experts and volunteers to refer to the overall RCCE framework
3. Decision makers in national and local governments, response partners and donors to identify and support key aspects of RCCE work

This document is not a guideline, or a how-to, and should be used as a reference and resource to support localized strategies, micro-plans and actions to protect at-risk populations from yellow fever and to contain and control the outbreak.

As the outbreak evolves, this document will be updated and supplemented. The most-up-to-date information and versions can be found at www.riskcommunication/yellowfever.

2016 yellow fever outbreak in Africa
A yellow fever outbreak was detected in Luanda, Angola late in December 2015. Subsequently, a rapid increase in the number of cases has been observed in Angola and neighbouring countries. Despite extensive vaccination campaigns in several Angolan provinces, circulation of the virus persists.

In addition, three countries have reported confirmed yellow fever cases imported from Angola in Democratic Republic of the Congo (DRC), Kenya, People’s Republic of China and Uganda.

Yellow fever virus is transmitted by the Aedes mosquito, which also transmits chikungunya, dengue and Zika. The yellow fever vaccine remains the most important means to combat yellow fever. A full dose of the yellow fever vaccine provides immunity for life.¹

An Emergency Committee (EC) regarding yellow fever was convened by the Director-General of the World Health Organization under the International Health Regulations (2005) (IHR 2005) on 19 May 2016. The Committee Members decided that the current yellow fever outbreak did not constitute a public health emergency of international concern (PHEIC), however, they strongly emphasized the serious national and international risks posed by urban yellow fever outbreaks and offered technical advice on immediate actions for the consideration of WHO and Member States in the following areas:

¹ The amendment to Annex 7 of IHR (2005) entered into force and is legally binding upon all IHR States Parties as of 11 July 2016.
- the acceleration of surveillance, mass vaccination, risk communication, community engagement, vector control and case management measures in Angola and DRC;
- the assurance of yellow fever vaccination of all travellers, and especially migrant workers, to and from Angola and DRC;
- the intensification of surveillance and preparedness activities, including verification of yellow fever vaccination in travellers and risk communication, in at-risk countries and countries having land borders with the affected countries.

WHO and partners published a Yellow Fever Strategic Response Framework and Joint Operations Plan (2016) to guide the international response to the yellow fever outbreak in Angola, DRC and other countries at risk.
RCCE Building Blocks
Based on the recommendations of the Emergency Committee regarding yellow fever this paper, developed collectively by WHO, UNICEF and partners, provides guidance to personnel and volunteers engaged in risk communication and community engagement in support of the response to the ongoing yellow fever outbreak in Africa.

The following RCCE model is proposed.

1. Vaccination
The key priority at this stage is to get everyone living in affected communities to get vaccinated against yellow fever. By the end of June 2016, more than 19 million doses of the vaccine have been shipped to Angola, DRC and Uganda for the current outbreak.

The yellow fever vaccine is safe and effective. It can be administered to adults and children above the age of 9 months. During an outbreak, vaccination is administered for children above the age of six months, and pregnant women. A single dose of the yellow fever vaccine provides life-long immunity against the disease. The vaccine becomes effective 10 to 14 days after it is administered and after 30 days, it provides full life-long immunity. Vaccinations must always be accompanied by knowledge of when to seek care and access to health services, and how to use personal protection against mosquitoes, including vector control (see section below). This is especially important before and during the two weeks after vaccination. To prevent outbreaks in affected regions, vaccination coverage must reach at least 80% of the population at risk with people sensitized about the importance of keeping their vaccination card or record.

It is critical that appropriate communication and engagement strategies and capacities are in place to support outbreak response immunization activities. Risk communication plans must address any misconceptions and rumours related to immunization in a timely and targeted manner. Health care
providers, traditional healers, religious leaders, community based organizations (CBOS), local and public authorities should be engaged to educate their community on the safety, affordability (vaccines are free), and access of the yellow fever vaccine. Communities should be engaged in micro-planning and implementation of the vaccination campaign. These groups can also be engaged to show public support to the vaccination campaign, and help monitor progress. Advocacy among religious and other local leaders is effective and key to promoting awareness on about the importance of immunization. Local and religious leaders, including traditional healers, should also be specifically sensitized through workshops and briefings to support the vaccination campaign.

National and local media outlets, community radio, text message campaigns and social media are indispensable channels to communicate and disseminate information in a timely, transparent and flexible manner and contribute to building trust and seeking feedback to inform the evolving yellow fever response. It is essential to build and maintain trust in the response operation, especially the vaccination campaigns to ensure communities at risk are protected through vaccination and the outbreak is brought under control. Effective RCCE work is central to this.

Limited vaccine stocks
Yellow fever vaccination is routinely carried out in 20 countries. WHO, UNICEF, MSF and IFRC manage a global YF vaccine stockpile to quickly supply additional vaccines during outbreaks. This emergency mechanism, known as the International Coordinating Group on Vaccine Provision (ICG), is a core component of the international response to contain yellow fever, meningitis and cholera outbreaks. The ICG maintain a stock of 6 million yellow fever vaccines. However, the 2016 yellow fever outbreak, first in Angola and now in DRC, has taken place in dense urban settings, and the number of vaccines required is unprecedented. Together with partners, countries and vaccine manufacturers, the global stockpile has been replenished three times between January and June 2016 and more than 19 million vaccines have been sent to affected countries and areas. With the outbreak threatening to spread further, and because it takes six months to produce a yellow fever vaccine, there are currently not enough vaccine supplies to protect all those at most-risk. This has necessitated a vaccine sparing strategy including the use of the existing yellow fever vaccines in a different way, using a fractional or emergency dose for this particular outbreak.

Fractional dosing of yellow fever vaccines
On 17 June, WHO Strategic Advisory Group of Experts (SAGE) on Immunization met and reviewed existing evidence to determine the feasibility of using fractional dosing--also referred to as dose sparing--in the context of a potential vaccine shortage.

The expert committee noted that using a fifth of a standard vaccine dose would still provide protection against the disease for at least 12 months. More research is needed to find out whether fractional doses would be effective in young children, who may have a weaker immune response to yellow fever vaccine. Dose sparing strategy is considered an emergency method in cases where there is a severe yellow fever outbreak combined with insufficient vaccine supplies. This dose sparing strategy is implemented based on a comprehensive risk assessment in close collaboration the national ministry of health of the countries concerned. In August 2016, WHO and UNICEF will launch a yellow fever vaccination campaign using fractional doses in the DRC as an emergency measure to address the current outbreak.
In any setting where an emergency or factional is considered, RCCE is very important in order to gain acceptance and understanding at all levels, from government leaders, to health care workers and the communities in order to dispel rumours and misinformation. People need to understand that this is the same yellow fever vaccine as routine immunization, but in a smaller quantity or dose and that the protection against the disease will be for at least one year, with a view to revaccinate with a full dose as more vaccines become available. More guidance on RCCE and concrete information on fractional dosing will be included as the situation evolves and be provided to field teams before vaccination campaigns using the fractional dose (see Resources).

**Key challenges**

1. Demand exceeds supply: Vaccination campaigns are being rolled out in affected countries and localities. However, limited global vaccine stocks and logistical and practical challenges, has slowed down delivery of vaccination. An additional challenge is ensuring vaccine availability at health centres for those who miss the campaigns⁴.

The dose sparing strategy in Kinshasa, DRC is being implemented while WHO and UNICEF continue to work with manufacturers to step up vaccine production. In parallel, a RCCE strategy is being revised to support communication efforts to explain and implement this approach to local populations.

2. Vaccine hesitancy: Vaccine hesitancy is the delay in acceptance or an outright refusal of vaccines despite availability of vaccination services and remains a concern. There is a general trend globally in people’s reluctance to use vaccines and this is supported proactively by the “anti-vaccine lobby”. There can be many reasons for this. In Angola, this trend appears to be higher in men. Other reasons for vaccine hesitancy include fear that the vaccine is dangerous, unwillingness to wait in long lines for vaccination, and reports that there is a fee for receiving the (free) vaccine.

3. Proof of vaccination as a requirement for international travel: This is a potential challenge as experts consider the use of fractional dose. The logic is that a fractioned concentration of the vaccine can still provide protection against yellow fever for up to at least a year and is an effective strategy in an emergency situation such as that in Angola and DRC. However, the use of fractional dose has led to questions on whether people receiving a yellow fever vaccine given at a dose as low as one fifth of the regular dose will be allowed to travel internationally. It has been made clear that people vaccinated with a fractionated dose will not receive a yellow fever certificate, which allows for travel, as required under the International Health Regulations (IHR 2005), but will receive another record of vaccination with the fractional dose.

4. Myths and rumours: Outbreaks usually bring to the surface myths and rumours that already exist. Fears about safety of vaccines are already on the rise in outbreak areas, with rumours circulating about reported deaths and serious adverse events following immunization (AEFI). In some cases, people are distrustful of the vaccine being used in the yellow fever vaccination campaigns. One reason often cited is that the packaging looks different. There is also underlying distrust that is fuelled in part, by vaccine shortages and general lack of understanding of the rationale behind prioritizing and phasing geographical areas and groups for vaccination.

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⁴ For example, in Angola, in February 2016, as many as 14% of men surveyed by CDC claimed they were travelling during the vaccination campaign in their district and did not know that they could continue to get the vaccine at a local health center even after the campaign was over.
5. Lack of adequate and timely social mobilization around vaccine campaigns: Due to global vaccine shortage, the doses are arriving in batches, campaigns are being run simultaneously, in multiple districts at the same time at short notice, therefore not allowing adequate lead time to plan and conduct social mobilization efforts. As a result, social mobilization efforts are not always integrated into vaccine micro planning. Improved coordination in micro planning is required, and time for social mobilization to occur in new areas is a must to ensure coverage.

3. Patient care

Laboratory diagnosis is required to confirm yellow fever virus infection. Symptoms of yellow fever are non-specific and resemble other tropical febrile diseases. After 3–6 days’ incubation period, it typically starts with sudden onset of fever and symptoms include headache, backache, general muscle pain, prostration, nausea and vomiting. Slow pulse, out of proportion to the elevated temperature (Faget sign), may be observed. Within a week, most symptoms resolve but in approximately 15 % of patients, following brief remission of hours to a day, initial symptoms recur and progress to jaundice and haemorrhagic symptoms (toxic phase).

Case-fatality can be very high: from 5% to 20% for patients with jaundice and, in the absence of supportive care, up to 50% of severe cases, commonly 7-10 days from the onset of initial symptoms. Patients with severe yellow fever disease need good supportive care such as the management of symptoms, maintenance of fluid balance and the monitoring of laboratory parameters. Symptom relief include the control of fever and pain (paracetamol), but Salicylates (aspirin ®) should NOT be used to minimize bleeding. In epidemic countries, patients with suspected yellow fever with progressive or severe symptoms should be hospitalized and receive good supportive care. All patients should be provided with impregnated mosquito nets and receive health education for their use during day time as well as night time, to prevent health facilities to become a source of infection.

RCCE efforts should include transfer of knowledge about yellow fever transmission, symptoms and encourage early health care seeking behaviour. Those with symptoms should be encouraged to visit the nearest health centre, clinic or hospital. Health care workers must receive clear information, communication and training about identifying and managing people suspected to have yellow fever, as well as their role in surveillance and notification so that the outbreak can be tracked and managed.

Key challenges

1. Yellow fever may be confused with other illnesses. Differential diagnosis include: severe malaria, dengue haemorrhagic fever, leptospirosis, viral hepatitis, other haemorrhagic fevers, as well as poisoning. Patients living in malaria-endemic areas, may confuse symptoms of yellow fever as those of malaria and self-medicate with anti-malarials, which has severe negative consequences.

2. Many endemic countries suffer low access rates for health care centers. Additionally, the sick prefer to seek care from traditional healers rather than from trained health or medical workers, thereby increasing the patient’s risk of progressing to severe illness. Seeking

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3 Especially the fulminating forms of hepatitis B and D
medical care in a health center is equally important for disease reporting and case referrals which need to be addressed through community engagement.

3. Treatment of patients with severe yellow fever disease is resource intensive requiring additional medical supplies and trained medical staff, which may not be readily available or accessible in countries currently experiencing outbreaks in Africa.

3. Vigilance at border crossings and points of entry (POE)
Yellow fever has already started to spread across borders and internationally, to China and Kenya, and the across land borders to DRC. This highlights the need for effective risk communication at border crossings and points of entry (POE). The use of all relevant national and local languages become essential, and easy to understand visual images, posters, radio announcements are needed on both sides of national borders. There must be capacity to inspect vaccination cards and share information on where to seek care and how to access vaccination

Key Challenges
1. Porous national borders: Porous borders, especially between Angola and DRC, make it very challenging to control population movements. Where border officials are stationed, they often have a lack knowledge and training on yellow fever certificate verification processes. Additionally, border control officials have no training on communicating the need for the yellow fever certificate and country specific travel regulations.

2. Fake vaccination cards: There have been reports of fake vaccination cards in circulation, particularly at the border areas.

3. Border communities: Population groups with families living on both sides of national borders require special attention and coordinated communication efforts to ensure that they are aware of the respective countries public health regulations regarding yellow fever. Border populations will also avoid checkpoints if they are unvaccinated or do not have vaccination cards. These communities rarely have access to health care and emergency medical services. Risk communications activities will have to tailor messages about where these groups can seek patient care and how this impacts surveillance.

4. Personal protection & integrated vector control
Controlling the Aedes vector which spreads yellow fever as well as other prevalent diseases such chikungunya, dengue and Zika is important. Current yellow fever outbreaks are occurring in urban settings with high population numbers and density with suboptimal housing and environmental sanitation, poor access to and management of community and household water and low routine immunization coverage. In addition, personal protection measures are critically important for at-risk groups, such as those for whom the yellow fever vaccination is contraindicated (infants under 9 months), pregnant women, people with severe allergies to egg protein, and people with severe immunodeficiency.

Areas with dense populations also put additional strains on an already constrained vaccine supply situation. In addition, many of the countries experiencing yellow fever currently also have a high disease burden of malaria (a reported 30% rate of co-infection in Angola).
In Angola, DRC and other countries where dengue and malaria co-exist with yellow fever, personal protection and integrated vector control measures for both day and night should be promoted at all times.

Personal protection measures include wearing protective clothing, sleeping under insecticide treated bed nets even during the day and using recommended repellents. Where possible, screens should be placed over openings such as windows in buildings especially health facilities. These measures also provide extra protection to all people who live in countries where Aedes and Anopheles coexist.

The key personal protection message must be “protect yourself from mosquito bites, day and night.” Advocacy and social mobilization efforts should also be strengthened in the lead up to, and during mass vaccination campaigns, particularly as the vaccine is only effective 10-14 days after it is administered.

Vector control for both Aedes and Anopheles need to be prioritized—mosquito breeding sites have to be identified and managed and adult mosquitoes killed. This includes killing adult mosquitoes by using insecticides in areas with high mosquito density and getting rid of mosquito eggs and larvae by removing mosquito breeding sites. Government and local municipal teams are responsible for management and supervision for chemical vector control by using fogging or using larvicides and through routine collection of garbage. However, it’s not sufficient to rely only on environmental vector control. Community involvement through activities such as cleaning household drains, water pots, covering water containers and any other places where there is even a small amount of stagnant water in and around the house where mosquitoes can breed is a very important and effective way to control mosquitoes. Vector control activities provide a basis for community engagement and social mobilization which can help the other building blocks of the RCCE approach. Therefore, it is essential to carry out integrated vector control to complement other programmes and interventions.

Key challenges
1. Stagnant water and water collections around densely populated households make vector control challenging. This is compounded where environmental sanitation is poor.
2. Ensuring sustained community involvement in vector control in and around the house is not easy as it requires commitment to clean the surroundings and getting rid of stagnant water on a regular basis.
3. Scarcity of human and financial resources may require prioritization of geographical areas for vector control based on entomological and epidemiological/social data
4. Yellow fever is just one of several arboviruses spread by the Aedes mosquito (that bites predominantly during daylight hours). Chikungunya, dengue and Zika are also spread by the same mosquito.

RCCE Strategies and Focus
Raising public awareness, demand for vaccination through behaviour change communication and social mobilization for priority communities, and engaging populations early on in response strategies are critical for the control of yellow fever outbreaks. At risk populations have a right to, and need information adapted to their local context, in their local languages about yellow fever.

July 2016
including symptoms, mode of transmission, need for vaccination, seeking medical care early, vector control and other protective strategies. Risk communications strategies should be based on the analysis of socio-cultural and gender barriers to adopt interventions (e.g., vaccine hesitancy, vector control, seeking medical care, etc.).

Operational social sciences research (rapid Knowledge, Attitude and Practice (KAP) surveys and focus groups, interviews and observation studies around vaccines acceptance, environmental and personal protection should be implemented to understand barriers and supportive practices to applying communication interventions, especially where reactive mass vaccination campaigns are being planned and implemented. The early engagement of community influencers and proactive listening by grassroots level actors (mobilisers, health workers) and planners, to identify and address misinformation and rumours are essential. Operational research also can help to identify vulnerable groups and specific strategies to address their needs.

For the purposes of this guide, countries have been divided into three broad categories according to their risk of a yellow fever outbreak:

- Countries with a current outbreak
- Countries that share a border with a country experiencing a yellow fever outbreak, and other countries where yellow fever is endemic
- Other countries at risk of importation through international travel/trade, and at risk of outbreak due to presence of *Aedes* mosquitoes.

**Countries experiencing an outbreak:** Rapid formative studies, even after an initial emergency response campaign to vaccinate against yellow fever, should be conducted to inform national risk communication and community engagement strategy, with micro-plans developed for those regions/districts with the current yellow fever outbreak to promote vaccination as a first resort for prevention. Based on the research, the national risk communication and community engagement strategy will outline use of locally relevant media, social and community mobilization and local level advocacy to ensure all population eligible for the vaccine are immunized. Risk communication should manage fear, traditional beliefs against vaccines and other concerns to address poor uptake.

Communication plans should also take into account the possibility of over demand for the vaccine from non-outbreak communities. Given the current shortage of vaccines globally, it is recommended that in non-outbreak regions or those not considered high risk and therefore not prioritized for an immunization response within an outbreak country, communication interventions should prioritize environmental health, personal protection and community and household vector control, especially for protecting non-targeted population and pregnant women.

In order to manage the communication response, relevant ministry of health authorities should set a risk communication and social mobilisation coordination mechanism, and develop and carry out continuous assessment of the adequacy of community engagement strategies, focusing on analysing public concerns and knowledge gaps and providing feedback and accountability to affected populations with regards to the on-going outbreak.

Communication materials developed internationally or nationally should be adapted to local cultural perceptions and languages and community health workers, mobilisers, volunteers and health
workers should be trained on key messages and, if needed, on interpersonal communication skills. Supervision of and reporting by actors engaged in risk communication activities should be ensured.

Risk communication relating to vector control should engage communities, families and individuals through health education and social mobilization informed by KAP assessment/ action research to tailor strategies and messages. Partners should facilitate the development and implementation of community-led action plans and community monitoring mechanisms.

Preparation and dissemination of messages on vaccine and vaccination campaigns should be based whenever possible on the results of KAP surveys, focus group discussions, and rumour monitoring to identify and address vaccine hesitancy. Key stakeholders include communities, families and individuals but also influential individuals and community leaders, CBOs, religious groups, CSOs and professional groups, services providers and local authorities. Risk communication on health-seeking behaviour so as to prevent delays in access to care is based on educating communities, families and individuals as well as community health workers and other health care providers, including traditional healers. Micro-plans should integrate risk communication and social mobilisation activities at local level.

**Countries that share a border with a country experiencing a yellow fever outbreak:** Addressing the risk of cross-border transmission from neighbouring countries should primarily focus on disease recognition and health seeking behaviour at the early stage of the disease through health education targeting communities, families, individuals, community health workers, health care providers, especially those living near, and crossing country borders frequently. All information should be made available at each POE in the country in relevant local languages.

Health authorities should develop and carry out continuous assessment of community engagement strategies, and news and social media monitoring, focusing on analysing public concerns and knowledge gaps with regards to the yellow fever outbreak. Information, education and communication materials should be adapted to local cultural perceptions and languages. Preparation and dissemination of messages on vaccine and vaccination campaigns should be based whenever possible on the results of KAP surveys, of focus group discussions (FGDs), rumour monitoring to identify and address vaccine hesitancy. Key stakeholders include communities, families and individuals but also influential individuals, leaders.

Risk communication on health seeking behaviour so as to prevent delay in access to care is based on health education to communities, families and individuals as well as to community health workers, and health care providers, including traditional healers. The focus should be on informing the population on identification of signs and symptoms, to start oral rehydration and paracetamol early, referrals and location of vaccination and care seeking services. Vector control and personal protection through maintaining clean environment, households and hygiene should also be prioritized. The material used for community engagement as well as preparedness plans should be reviewed urgently especially in countries neighbouring those in epidemic stage. The population should be informed on disease symptoms, on the risk of outbreak and on where to get treated in case of illness.

**All other countries:** Authorities should ensure that the minimum of information is made available at least at main entry points to travellers and border control officials using communication, briefing and infographics products, disseminated by mass media and social media. **Travellers likely to travel**
to an affected country/area should be made aware of the need for compulsory vaccination at least 10 days prior to departure. Travellers returning from affected areas and countries should be informed on clinical presentation of yellow fever and on how and where to report in case of suspicion of infection.

At regional and global level: Risk communication and community engagement tools and products adapted to yellow fever should be made available to countries and partners and surge capacity deployed as needed. Key issues such as dose sparing strategies, vaccine stockpile and shortages and how to communicate multiple risks by vector borne diseases concurrently in the same region (Zika and yellow fever) need to be addressed at the global level. Wherever possible, key operational partners should coordinate their messages and activities for greater effect and consistency. Risk communication tools and strategies for health care providers and other key stakeholders should be developed and disseminated including though the use of technology. Journalists networks should be mobilized to educate them on key issues related to the YF outbreaks including information and education on vaccination and its key issues such as the use of the fractionate dose.
Facts, Key Messages and Recommended Behaviours for RCCE Practitioners

Facts about yellow fever and its signs and symptoms

- Yellow fever occurs in 47 endemic countries in Africa in Central and South America. Around 90% of cases reported every year occur in Sub-Saharan Africa.
- Yellow fever is an acute viral haemorrhagic disease transmitted by infected mosquitoes. The "yellow" in the name refers to the jaundice that affects some patients.
- Infected mosquitoes transmit yellow fever virus, the most common being the Aedes species – the same mosquito that spreads the Zika, chikungunya and dengue viruses.
- Haemogogus mosquitoes also spread yellow fever and are mostly found in the jungle. Mosquitoes become infected with the virus when they bite an infected human or monkey.
- Mosquitoes carrying yellow fever virus breed in tropical rainforests, humid, and semi-humid environments, as well as around bodies of still water in and close to human habitations in urban settings. Increased contact between humans and infected mosquitoes, particularly in urban areas where people have not been vaccinated for yellow fever, can create epidemics.
- Outbreaks of the disease are of particular concern when they occur in overcrowded settings with inadequate water supply and waste management services that allow the mosquitoes to breed easily.
- Infected travellers from areas where yellow fever occurs can export cases to countries that are free of yellow fever, but the disease can only spread easily if the destination country has the mosquito species able to transmit it, specific climatic conditions and the animal reservoir needed to maintain it.
- Symptoms of yellow fever include: fever, headache, jaundice, muscle pain, nausea, vomiting and fatigue.
- Symptoms of yellow fever can be confused with those of malaria, dengue or other illnesses so always seek medical treatment and care.
- Yellow fever cannot be spread by contact from one person to another.
- Some infected people experience a second, more severe phase of illness, which includes high fever, jaundice and internal bleeding. At least half of severely affected patients who don’t receive treatment die within 10 to 14 days.

For outbreak and endemic countries and countries where yellow fever vaccination is provided

Facts and key messages on prevention, vaccination and potential side effects

The yellow fever vaccine is the most effective prevention against yellow fever.

- A full doze of yellow fever vaccine provides lifelong immunization against the disease.
- The following populations should be excluded from vaccination:
Infants aged less than 9 months, except during an epidemic when infants aged 6-9 months, in areas where the risk of infection is high, should also receive the vaccine; 
Pregnant and/or breastfeeding women – except during a yellow fever outbreak when the risk of infection is high; 
People with severe allergies to egg protein; and
People with severe immunodeficiency due to symptomatic HIV/AIDS or other causes, or who have a thymus disorder.

- Side effects from yellow fever vaccination are rare. The rates for severe side effects or ‘adverse events following immunization’ (AEFI), are between 0.4 and 0.8 per 100 000 people vaccinated.
- The risk of side effects is higher for people over 60 years of age and anyone with severe immunodeficiency due to symptomatic HIV/AIDS or other causes, or who have a thymus disorder.
- People over 60 years of age should undergo a careful risk-benefit assessment to determine if it is safe to receive the vaccine.
- Anyone planning to travel to and from yellow fever endemic and epidemic countries must be vaccinated at least 10 days prior to travel and present a yellow fever vaccination certificate for verification upon entry to the corresponding country.
- WHO and partners will support governments to play a direct and pre-emptive role in implementing vector surveillance and vector control at the scale needed to prevent transmission.

For outbreak countries that employ fractional dosing of the yellow fever vaccine

**Facts and messages about temporary use of fractional dosing of yellow fever vaccine**

- Fractional dosing or dose sparing is being used as an emergency, short-term measure to control an outbreak in DRC because vaccine supply is limited.
- Studies show that the yellow fever vaccine, given as one fifth of the regular dose still provides full immunity against the disease for at least 12 months.
- The fractional dose comes from the same full dose vaccine. It has been given to millions of people to prevent yellow fever in the past. It is as safe and as effective as the full dose of the vaccine.
- This approach is not proposed for routine immunization, as there is not enough data available to show that lower doses would confer life-long protection as provided with one full dose of the vaccine.
- The DRC with WHO and partners’ support are planning a vaccination campaign using fractional dosing in the city of Kinshasa, which has an estimated population of 10 million people and reported cases of yellow fever.
- Using fractional dosing is the best way to stretch vaccine supplies and protect as many as 8 to 10 million people as soon as possible to stop the spread of yellow fever before the long rainy season begins in October.
- This fractional dose will not entitle people to a yellow fever certificate valid for international travel.
- People who travel internationally, require a full dose of the vaccine. The full dose provides life-long immunity and entitles them to an international yellow fever certificate.
- Children under two years of age will be offered a full dose of the vaccine.
- Countries must keep good vaccination records of people receiving the fractional dose so that they can be followed up later to assess how long the vaccine protection lasts and be revaccinated if necessary. These people will need to be informed that they have received the fractional dose and will require a full dose of the vaccine if they wish to travel.
- As soon as the current outbreak is brought under control, the full dose of the vaccine should be used in routine vaccination programmes. People who received a fractional dose may need a booster vaccination later.
- Severe adverse effects following a full dose of yellow fever vaccine are extremely rare (less than one per one million people). There is no evidence of increased severe adverse effects when using a fractional dose.

For countries experiencing outbreak and any country with presence of *Aedes* mosquitos

*Vaccination against yellow fever is recommended for the entire population, including children above 9 months of age. Some adults and children cannot be vaccinated as explained above.*

**Personal Protection Messages**

- Use insect repellent. When outdoors, use an EPA-registered or its equivalent insect repellent such as those containing DEET, picaridin, IR3535, or oil of lemon eucalyptus on exposed skin. Even a short time outdoors can be long enough to get a mosquito bite.
- Wear proper clothing to reduce mosquito bites at all times. Mosquitoes may bite through thin clothing, so spraying clothes with repellent containing permethrin or another EPA-registered repellent will give extra protection.
- Be aware of peak mosquito hours. The peak biting times for many mosquito species is dusk to dawn. However, *Aedes aegypti*, one of the mosquitoes that transmits yellow fever virus, feeds during the daytime. Take extra care to use repellent and protective clothing during daytime as well as during the evening and early morning.
- Stay or set up accommodation with screens or air-conditioned rooms, particularly during peak biting times. Both AC and screens can reduce risk of mosquito bites.
- Insecticide-impregnated mosquito nets should be used in health facilities as part of the management of suspected cases of yellow fever.

**Vector Control Messages**

- Always keep stored water in covered containers. Containers used to store water should be cleaned, scrubbed, and emptied at least once a week, to eliminate any mosquito eggs that may be in these containers.
- Drain any containers, garbage, and waste where water can collect in and around your home. If containers cannot be drained or dumped out, fill them with sand or cover them to prevent mosquitoes breeding sites.
- If there are broken or leaky pipes at home or in the community, repair the pipe and/or report it immediately to authorities to prevent stagnant water.
• Report mosquito breeding grounds in public spaces or the workplace to appropriate authorities, and cleaning areas where mosquitoes breed.
• Lead or join community actions to eliminate mosquito breeding sites. Always wear protective clothing and insect repellents when engaged in eliminating breeding sites.
• Speak to and support local/public authorities to treat the outdoors and surrounding areas of your house with insecticide to kill adult mosquitoes.
• Eliminate stagnant water and treat water storage containers with larvicides to kill larvae and eggs in the following areas:
  ➢ Public spaces and other areas (e.g. tire shops, scrap yards, etc.) should be surveyed and cleared of any breeding sites.
  ➢ Places of mass gathering (e.g. community centres, health care centres, places of worship), where water is stored should always be covered and cleaned regularly, at least once a week.
• Engage with leaders, teachers, and managers of public places where people gather to eliminate mosquito breeding sites and disseminate information about preventive behaviours. Have local call to actions to improve environmental sanitation or promote “clean up days”
• Engage in mass media and social media activities aimed at children and parents to promote key preventive behaviours.

For travellers to and from yellow fever endemic and outbreak countries

• Vaccinate at least 10 days prior to departure for international travel.
• Keep the yellow fever vaccination certificate as proof of life-time immunity
• Recognize the signs and symptoms of yellow fever, seek immediate medical care in case of suspected infection.
• Prevent mosquito bites (see above).
• Be diligent in the use of higher percentages of active ingredient that provide longer protection. Use products with the following active ingredients:
  o DEET (Products containing DEET include Off!, Cutter, Sawyer, and Ultrathon)
  o Picaridin (also known as KBR 3023, Bayrepel, and icaridin), products containing picaridin include Cutter Advanced, Skin So Soft Bug Guard Plus, and Autan [outside the US]5
  o Oil of lemon eucalyptus (OLE) or PMD (Products containing OLE include Repel and Off! Botanicals)
  o IR3535 (Products containing IR3535 include Skin So Soft Bug Guard Plus Expedition and SkinSmart)6
• Cover exposed skin by wearing long-sleeved shirts, long pants, and hats.
• Stay alert for mosquito breeding sites and either destroy them or inform those responsible

Facts and Messages for Patient Care

5 EPA Pesticides. Link: https://www.epa.gov/pesticides
Yellow fever is difficult to diagnose, especially in the early stages. Symptoms can be confused with those of severe malaria, leptospirosis, viral hepatitis, and other haemorrhagic fevers including dengue.

Many people do not experience symptoms but when they occur, the most common are fever, muscle pain, prominent backache, head ache, loss of appetite, and nausea or vomiting.

There is no specific treatment for yellow fever, but good and early supportive treatment can improve the outcome of patients.

Specific care can be provided to treat dehydration, fever, and liver and kidney failure. Associated bacterial infections can be treated with antibiotics.

A small percentage of patients can enter a more toxic phase within 24 hours of recovering from initial symptoms. High fever returns and several body systems are affected, usually the liver and kidneys. In this phase patients develop jaundice (yellowing of the skin and eyes), dark urine and abdominal pain with vomiting. Bleeding can occur from the mouth, nose, eyes or stomach.

Facts and Messages for Border Control and Points of Entry

- Yellow fever vaccination is a requirement for all travellers entering areas where there is a yellow fever outbreak or where the disease is endemic according to the International Health Regulations (IHR 2005).
- This measure is required to protect individual travellers who may be at risk of yellow fever infection and to prevent the international spread of the disease.
- To prevent international spread of yellow fever, proof of vaccination is required for travellers arriving and leaving countries where there is a yellow fever outbreak or where the disease is endemic.
- All travellers to and from yellow fever outbreak or endemic areas of above 9 months old have to present border control officials with a proof of yellow fever vaccination (vaccination card).
- Refer to the national/local policies for specifics in dealing with travellers who do not present with a yellow fever vaccination card at border control.
Resources

Public Health Response:

Yellow Fever Strategic Response Framework and Joint Operations Plan (2016)

Interactive Timeline of the Yellow Fever Outbreak 2016

Yellow Fever Vaccination:

Q&A on Yellow Fever

Q&A on the International Coordinating Group on Vaccine Provision

Video Q&A on the Yellow Fever Vaccine Stockpile

Yellow Fever Stockpile in Emergencies

Statement on Fractional Dosing

Q&A on Fractional Dosing

Communication and social mobilization in yellow fever mass vaccination campaigns: 10 points from field experience
Key response documents
YELLOW FEVER
STRATEGIC RESPONSE PLAN
JUNE-AUGUST 2016

Yellow Fever Strategic Response Plan
11/07/2016
WHO/YF/ENB/16.2 Rev.1
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This document is intended to guide a coordinated international response to interrupt transmission of the 2016 yellow fever outbreak in Angola, the Democratic Republic of the Congo, and a concurrent yellow fever outbreak in Uganda, including preparedness for the importation of cases in non-affected countries. The document is informed by lessons learned over the past six months, and provides an overview of the current situation, outlining the response strategy for the rapid containment of current outbreaks and the prevention of international spread. It includes a Joint Operations Plan that provides further detail of how WHO and its partners are and will continue to implement the framework’s strategic objectives.

The overview and strategy were developed with input from WHO’s regional office for Africa, the WHO Country Offices of Angola, the Democratic Republic of the Congo, and Uganda, and from partners including Médecins Sans Frontières, the Prevention and Control Program of the Communicable Disease Control Directorate of the Department of Health, Western Australia, UNDP, UNHCR, UNICEF regional offices for West and Central Africa (WCARO) and East and Southern Africa (ESARO), UNICEF headquarters, and from The University of Texas Medical Branch (UTMB Health).

**GOAL**
End yellow fever outbreaks in affected countries and limit international spread

**COORDINATION**

**SURVEILLANCE AND RISK ASSESSMENT**
**VACCINATION**
**CASE MANAGEMENT**
**VECTOR CONTROL**
**SOCIAL MOBILIZATION AND RISK COMMUNICATION**

**COUNTRY CONTEXTS**

- Countries with a current outbreak
- Countries that share a border with a country experiencing a yellow fever outbreak, and all other countries in which yellow fever is endemic
- Other countries at risk of importation through international travel and trade, and at risk of an outbreak due to the presence of Aedes spp. mosquitoes

**TOTAL REQUIREMENT**
US$ 94.1M
OVERVIEW OF THE SITUATION

Background

Yellow Fever is endemic in tropical areas of Africa and Central and South America. Thirty four (34) countries in Africa and thirteen (13) in Central and South America are either endemic for, or have regions that are endemic for, yellow fever.¹

On 21 January 2016 WHO received official notification through the International Health Regulations (2005) of a yellow fever outbreak in Angola.² The first suspected cases were reported in late December from Luanda – the country’s capital city and main trade and travel hub, with a population of over 6 million people. The disease, which is transmitted in urban settings by the Aedes aegypti mosquito, spread rapidly in Luanda. From there, cases were exported to the rest of the country (figure 1). By early May, all 18 of Angola’s provinces had reported suspected cases of yellow fever. As of 11 July, 12 provinces had confirmed local mosquito-borne transmission (figure 2). Cases of yellow fever have also been exported from Angola to the Democratic Republic of Congo (DRC), China³ and Kenya⁴ (figure 1; table 1).

On 22 March, the DRC, which borders Angola to the south, confirmed the detection of imported cases of yellow fever in areas bordering Angola by analysis at the Kinshasa National Institute of Bio-medical Research (INRB) and Pasteur Institute Dakar (IPD).⁵ By 15 June, over 63 confirmed cases had been reported in districts bordering Angola (figure 1), including evidence of local mosquito-borne transmission in the capital, Kinshasa, and the country’s main seaport Matadi. Together these two large urban settlements have a population of over 11 million people and are well connected to international travel and trade routes. On 21 May 2016, The Republic of Congo reported a probable case of yellow fever in the town of Madingou, located close to the border with DRC and Angola. WHO provided immediate technical assistance to the Congolese Ministry of Health, and is currently undertaking full field investigations to determine the nature and possible source of infection. As of 11 July, two probable cases were reported in The Republic of Congo. Resources have been mobilised to strengthen local surveillance and diagnostic capacity.

Table 1 | Total yellow fever cases and deaths as of 11 July 2016

<table>
<thead>
<tr>
<th></th>
<th>Total confirmed, probable, and suspected cases of yellow fever</th>
<th>Total deaths from confirmed, probable, and suspected yellow fever</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local transmission plus imported cases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angola</td>
<td>3552</td>
<td>355</td>
</tr>
<tr>
<td>DRC</td>
<td>1582</td>
<td>75</td>
</tr>
<tr>
<td>The Republic of Congo</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Uganda*</td>
<td>68</td>
<td></td>
</tr>
<tr>
<td>Brazil*</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Peru*</td>
<td>79</td>
<td>9</td>
</tr>
<tr>
<td>Imported cases only</td>
<td></td>
<td></td>
</tr>
<tr>
<td>China</td>
<td>11</td>
<td>0</td>
</tr>
<tr>
<td>Kenya</td>
<td>2</td>
<td>1</td>
</tr>
</tbody>
</table>

*Not epidemiologically linked to the outbreak that originated in Angola. Investigations are ongoing into suspect cases (not epidemiologically linked to the Angola outbreak) reported in Ghana (4 cases), Guinea (8 cases). To date, the situation remains stable and there are no updates for Chad (1 case) and Colombia (1 case)

As of 11 July, over 3500 suspected cases and over 860 confirmed cases have been reported from Angola, with 355 deaths. Over 1500 suspected cases have been reported from the Democratic Republic of The Congo (DRC), where there have been 68 confirmed cases and 75 deaths.

Three countries have reported confirmed cases of yellow fever imported from Angola:
- 11 cases in China
- 59 cases in the DRC
- 2 cases in Kenya
In addition to the yellow fever outbreak taking place in and around Angola, on 26 March WHO received official notification of a yellow fever outbreak in Uganda. By 11 July, 68 suspected and seven confirmed cases had been reported from three districts. Analysis of the genetic sequence of the circulating virus indicates that the Ugandan outbreak is not linked to the outbreak in Angola. Further unrelated outbreaks in South America in 2016 have been reported from Peru in April and Brazil in May (table one). One case was also reported in Colombia. WHO also continues to support countries in Africa with the verification and investigation of other suspected cases of Yellow fever - Ghana (four cases), Guinea (eight cases) Chad (one case) -- all of which were reported in June.

Response
Since the beginning of the outbreak, WHO and partners have supported the governments of Angola, DRC, and Uganda in their ongoing efforts to rapidly interrupt yellow fever transmission and strengthen measures to prevent spread across borders. WHO and its partners in the International Coordinating Group (ICG) for Vaccine Provision are managing an emergency stockpile supported by the Global Alliance for Vaccine and Immunization (GAVI). As of 20 May 2016, WHO has facilitated the procurement and delivery of over 14 million doses of yellow fever vaccine allocated through the ICG mechanism, for mass vaccination campaigns in Angola, DRC and Uganda. Funds amounting to approximately $US 2.24 million have been disbursed from the WHO Contingency Fund for Emergencies to further support national response efforts in affected countries. The response in Angola has also been supported by the Central Emergency Fund of the United Nations (CERF). Further CERF proposals are in process for DRC and Uganda. However, despite reactive mass vaccination campaigns in the Angolan capital Luanda and the provinces of Benguela and Huambo, new cases continue to be reported throughout Angola and around the border area with DRC and the Republic of Congo. By 15 June continued spread of yellow fever in Angola, including on the border with DRC, and the confirmation of autochthonous transmission in Kinshasa, DRC, prompted WHO to initiate a rapid, large-scale vaccination campaign to prevent further spread.

Rationale for a global response strategy

The continued spread of yellow fever in Angola, evidence of local transmission in DRC, and the threat of further international spread triggered WHO to activate its organization-wide incident management system on 22 April 2016. A reallocation of vaccine stocks through ICG mechanisms has provided a temporary boost to vaccine availability; however, current vaccine stocks are insufficient to respond to multiple simultaneous urban outbreaks. In the context of a constrained global supply of yellow fever vaccine there is an urgent need for a coordinated global response in order to end current yellow fever outbreaks. Failure to intervene decisively now may result in further large-scale urban outbreaks in at-risk areas, and a consequent inability to meet the demand for vaccine. The strategic framework set out in this document provides the basis for WHO’s continued response to the yellow fever outbreak, and for strengthened coordination and collaboration with partners to ensure that national and international response activities are supported.

The Yellow Fever Emergency Committee gathered under the International Health Regulations (2005) convened by WHO on 19 May 2016 emphasized the seriousness of the national and international risks posed by urban yellow fever outbreaks and made the following recommendations:

- In Angola and DRC, accelerate surveillance, mass vaccination, risk communication, community mobilization, vector control and case management measures
- For travelers to and from Angola and DRC ensure travellers, especially migrant workers, are vaccinated against yellow fever
- In at-risk countries and countries that share land borders with affected countries, intensify surveillance and preparedness activities, including verification of vaccination of travelers and risk communication
- Identify and manage imported cases rapidly
- Evaluate the effectiveness of the response
- Rapidly expand yellow fever diagnostic and confirmatory capacity
- Apply the policy of one lifetime dose of yellow fever vaccine
- Undertake a rapid evaluation and implement the of dose-sparing strategies in consultation with the WHO Strategic Advisory Group of Experts (SAGE) on Immunization

6 CERF Funding by Country (2016) - Project Detail Angola (01/01/2016 to 24/05/2016; last accessed 24 May 2016).

7 World Health Assembly Resolution WHA 67.13.
# STRATEGIC OBJECTIVES

To achieve the over-arching goal of ending yellow fever outbreaks in affected countries and limiting international spread, WHO will coordinate with partners to support countries to attain the following strategic objectives:

1. **End outbreaks in currently affected countries through vaccination and other public health measures**
2. **Prevent morbidity and reduce mortality through early case detection and strengthened case management**
3. **Prevent international spread**
4. **Prioritize research to improve access to yellow fever vaccine, and to improve the effectiveness of other prevention and control interventions**

## Country context

The implementation of interventions should be tailored to three country contexts (Table 2 and below).

- Countries with a current outbreak: Angola, Democratic Republic of the Congo (DRC), and Uganda.
- Countries that share a border with a country experiencing a yellow fever outbreak, and all other countries
  - in which yellow fever is endemic
  - other countries at risk of importation through international travel and trade, and at risk of an outbreak
  - due to infestation by Aedes spp. Mosquitoes

## Table 2 | Recommended yellow fever response interventions by country context

<table>
<thead>
<tr>
<th>Surveillance and risk assessment</th>
<th>Current yellow fever outbreak</th>
<th>Endemic or adjacent to outbreak</th>
<th>At risk of importation and Aedes spp present</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assess the risk of the spread or start of an outbreak*</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Prepare for the importation of (more) cases from another area or country</td>
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<tr>
<td>Ensure prompt and open information sharing in country and with the WHO and members states at risk through the IHR focal person</td>
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<tr>
<td>Strengthen case detection and reporting, including laboratory diagnostic capabilities</td>
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<td></td>
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<tr>
<td>Monitor the course of the epidemic and the outcome of interventions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaccination</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undertake reactive mass vaccination in areas where it is still likely to have an impact on the course of the outbreak, primarily in urban settings†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consider halting yellow fever vaccination provided through the expanded program of immunization, in order to prioritize the use of available vaccine for mass vaccination</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Case management</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prevent excess mortality among suspected and confirmed cases</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social mobilization and risk communication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Community engagement and social mobilization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk communication</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vector control</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intensify vector surveillance and control</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Achieving the strategic objectives will require coordinated implementation of a broad range of interventions, grouped here into: surveillance and risk assessment; vaccination; case management; social mobilization and risk communication; and vector control. Coordination with member states and partners remains essential to enable the implementation of all response activities. WHO will continue to monitor trends in affected and unaffected countries, and will adapt the strategic response framework on the basis of changing epidemiology and needs. WHO will support the implementation of preparedness activities in priority and at-risk countries at national and sub-national levels, and will support the assessment of surveillance and response capacity.

**Surveillance and risk assessment**

Effective yellow fever surveillance\(^a\) is critical to ensure that new cases and newly affected areas are identified quickly and that all data are transmitted to decision makers in a timely manner, which in turn enables the rapid implementation of response measures to contain outbreaks. Access to yellow fever vaccine from the ICG stockpile depends on laboratory confirmation of a case according to the standard case definition. Integrated arboviruses surveillance (epidemiological and laboratory) is a must where several mosquito-borne diseases are being transmitted especially when clinical presentation at the start is none-specific. Robust systems for transmission and management of data, including links between case investigation information and laboratory results are required.

Approximately 25 laboratories are able to test for Yellow Fever in Africa. In addition, there are two (2) international reference laboratories for Yellow Fever: the Pasteur Institute Dakar, Senegal, and the Arbovirus Branch at the Centers for Disease Control in Fort Collins, USA.

WHO will coordinate technical support to countries through the Global Outbreak Alert and Response Network (GOARN) and WHO collaborating laboratories to strengthen national surveillance capacity, and harness support from the Inter Agency Standing Committee Cluster System as required. Areas of support will include technical support for surveillance, case investigation and risk assessment; provision of reagents, personnel, and equipment; sample transport logistics; and the deployment of mobile laboratories where needed to expedite laboratory testing. Additionally, coordination structures will be established and strengthened to support national government efforts at national and subnational levels in areas with ongoing outbreaks.

**Panel 1 | Yellow fever case definition**

A suspected case is confirmed when, in the absence of recent yellow fever vaccination, yellow-fever-specific IgM is found in the serum, or when a fourfold or greater rise in IgG levels is found in PAIRED acute AND convalescent sera, or when yellow fever virus is isolated in cell culture or laboratory animals, or in case of positive postmortem liver histopathology, or when yellow fever antigens are detected in tissues by immunohistochemistry, or when yellow fever virus genomic sequences are detected in blood or organs by molecular diagnostic techniques such as Reverse Transcription Polymerase Chain Reaction (RT-PCR).

Preparedness strengthening activities, including risk assessments for spread, will target priority countries at risk of yellow fever importation from countries with on-going outbreaks. As of end of May 2016, the countries at risk of cross-border importation from epidemic countries, either through mosquito infestation or human travel and trade are:

- Neighbouring Angola: western Zambia, northern Botswana, and northern Namibia
- Neighbouring Congo: Gabon

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Neighbouring affected areas in DRC: the south of the Republic of Congo
Neighbouring affected areas in Uganda: eastern DRC, northern Rwanda, and northern Tanzania (through boat travel across Lake Victoria)

Risk assessments for yellow fever outbreaks must be carried out regularly and be based on the findings of case and outbreak investigation and of entomological investigations. Recommendations should account for local surveillance and response capacity, and set prioritise interventions and resource allocation on the basis of national and local context.

In countries experiencing an outbreak

- Yellow fever case-based surveillance should be implemented and/or strengthened. Synergy with the existing polio surveillance network should be sought where appropriate. Case-based investigation aims to establish vaccination status, differentiate between local transmission (autochthonous transmission) and imported cases, and document travel history and information regarding location of exposure.
- As per the requirements of the IHR (2005), affected countries should monitor yellow fever vaccination status of travelers through entry points.
- Reporting of yellow fever cases and the geographical extent of the outbreak should be done in accordance with the requirements of the IHR 2005.
- WHO and partners will support:
  - Dissemination and use of the standard case definition.
  - Case-based surveillance.
  - Strengthening of national or regional reference laboratories to improve capacity for diagnostic testing and reporting, and the shipment of specimens for validation and quality control.
  - Strengthen laboratory capacity in countries where they are limited
  - Support implementation of inter-country cooperation mechanisms for cross-border surveillance and outbreak investigation.

In countries at risk of importation through international travel and trade, and at risk of an outbreak due to infestation by Aedes spp. mosquitoes

Ad-hoc surveillance measures should be strengthened, especially in countries that have regular flight, road and boat connections with countries and cities affected by outbreaks. Entry screening of yellow fever vaccination status may be implemented at entry points for travelers coming from affected countries.

Vaccination

Vaccination is the most important measure for preventing yellow fever. The vaccine is safe, affordable, and provides effective immunity within 10 days for more than 90% of people vaccinated and within 30 days for 99% of people vaccinated. A single dose confers sustained immunity and life-long protection. Side-effects are rare and serious adverse events are rarely reported.\(^9\) The International Certificate of Vaccination is valid 10 days after vaccination. In a non-epidemic situation all individuals above 9 months are eligible to be vaccinated with the exception of women who are pregnant and/or breastfeeding, individuals who are severely allergic to egg or another vaccine component, and immunocompromised individuals. In an epidemic situation eligibility for vaccination is extended to infants aged 6 months and above and to women who are pregnant and/or breastfeeding.

WHO and its partners in the ICG for Vaccine Provision have activated the ICG mechanism for release of yellow fever vaccine from the emergency stockpile. Despite the reallocation of vaccine from the Expanded Programme on Immunization (EPI) to the global stockpile, stocks are insufficient to respond to several simultaneous urban outbreaks. Vaccine producers have been requested to accelerate vaccine production, and WHO will continue to work with partners to:

- prioritize the release of vaccine according to risk
- validate and adopt dose-sparing strategies to increase vaccine availability
- carry out other research and development related to vaccines

WHO is developing a strategy on how best to prioritise the use of vaccines in the event of simultaneous urban outbreaks and a depletion of global stocks. Meanwhile, national strategies for vaccination may include either reactive mass vaccination campaigns, preventive mass campaign based on risk assessment (e.g. in high-risk areas located near the affected countries), or targeted vaccination of travelers, depending on the country’s risk of an outbreak. In the event that vaccine stocks approach exhaustion, routine vaccination activities against yellow fever as part of the expended program of immunization (EPI) may have to be deferred.

**In countries that share a border with a country experiencing a yellow fever outbreak, and in all other countries where yellow fever is endemic**

- Countries should enforce the vaccination of travelers.
- WHO will work with countries to map areas at highest risk of importation, and prioritise areas for pre-emptive vaccination to mitigate this risk.
- In the context of limited availability of vaccines where the yellow fever immunization coverage is below 80%, preventive vaccination\(^{11}\) may have to be postponed until the global vaccine stock is adequately replenished, unless the assessed outbreak risk is estimated to be high.
- Micro plans for emergency mass vaccination should address the logistical organization of the campaign, crowd control, safe waste disposal, resources mobilization, social mobilization/risk communication, daily monitoring of outcome of the campaign and monitoring of Adverse Events Following Immunization (AEFI).
- WHO will support the implementation of preparedness activities at national and sub-national levels, and the assessment of surveillance and response capacity.
- National/regional checks must monitor vaccine availability, injection/safety material availability, the availability of vaccination cards, the capacity

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\(^{10}\) WHO. Surveillance of adverse events following immunization against yellow fever. Field Guide for staff at the central, intermediate and peripheral level. January 2010: http://www.who.int/csr/resources/publications/HSE_GAR_ERI_2010_1ENw.pdf.

of active and passive cold chain, and report findings to the yellow fever partnership.

- Strict border control measures must be implemented to verify the yellow fever vaccination status of all passengers who have travelled to countries with a yellow fever outbreak in the past **two** weeks.\(^\text{12}\)

**In other countries at risk of importation through international travel and trade, and at risk of an outbreak due to infestation by Aedes spp. Mosquitoes**

- Countries that implement yellow fever vaccination as part of the routine EPI program and receive vaccine through UNICEF, will receive staggered shipments to prevent the exhaustion of national vaccine stocks. Countries will receive shipments one month prior to depletion of vaccine stocks. Such shipments will include enough supply to cover two months of use.
- All countries are at risk of importation through international travel and trade. Therefore, travelers planning to visit yellow fever endemic and epidemic countries or returning from affected countries, should be vaccinated at least ten (10) days before to travel to the affected country or at least ten (10) days prior to return to a non-affected country.\(^\text{13}\)

**Dose-sparing strategy**

Dose-sparing, also known as fractional dosing, is under consideration as a short-term measure, in the context of a potential vaccine shortage for use in emergencies. WHO Strategic Advisory Group of Experts (SAGE) on Immunization reviewed existing evidence that demonstrates that using a fifth of a standard vaccine dose would still provide protection against the disease for at least 12 months and possibly much longer. More research is needed to find out whether fractional doses would be effective in young children, who may have a weaker immune response to yellow fever vaccine.

**Clinical management**

Symptoms of yellow fever are non-specific and resemble other tropical febrile diseases, making diagnosis in the absence of laboratory testing challenging at all phases of the disease. Around 15% of cases suffer relapse after an initial phase. The case-fatality rate in severe cases can reach 50%.

There is no specific cure for yellow fever. Case management is based on supportive care and provision of insecticide-impregnated mosquito nets, including for daytime use, to prevent transmission to other patients via infected mosquitoes at the site of treatment. Symptom relief can include therapies to control fever and pain (paracetamol), but non-steroidal anti-inflammatory agents such as salicylates (aspirin) should not be used to limit the risk of bleeding in severely affected patients. Treatment of patients with severe yellow fever disease is resource intensive, requiring additional medical supplies and trained medical staff. Further recommendations for the management of patients suffering bleeding signs can be found in WHO guidance for the clinical management of patients with haemorrhagic fever\(^\text{14}\) and more general guidance for clinical management of yellow fever patients are included in reference communicable disease manuals.\(^\text{15}\) The WHO-coordinated Emerging Diseases Clinical Assessment and Response Network (EDCARN) has been mobilised, and will provide technical support, training and mentoring of the health workers involved in the yellow fever response.

**In countries experiencing an outbreak**

- Patients with suspected yellow fever with progressive or severe symptoms should be hospitalized and receive good supportive care. Presumptive treatment should be guided by local disease epidemiology (e.g. malaria) to eliminate other common causes of similar symptoms, and laboratory diagnosis should be prioritized.
- Care/supportive treatments for patients with suspected and confirmed yellow fever should be made available free of charge.\(^\text{16}\)

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• Trained health workers at all levels should be provided with the case definition to detect cases early, provide initial supportive care, and to refer to appropriate follow up.
• The disease-management strategy should assess the presence of co-infections with other similar debilitating conditions that may include malaria or other arboviruses such as dengue. Where needed malaria and dengue rapid-detection tests should be made available to support differential diagnosis.
• Although isolation of patients infected with yellow fever is not part of usual recommendations (no human-to-human transmission has been described), case management can be optimized through the creation of designated specialized health units.
• Insecticide-impregnated mosquito nets should be provided in clinical settings and for people who rest during the day (pregnant women, infants, sick or bedridden individuals), especially in countries neighboring those currently experiencing yellow fever outbreaks. Malaria and dengue rapid detection tests should be made available to support differential diagnosis.
• WHO and partners will support the dissemination of emergency guidance for clinical management, supply needs, train staff and support case management activities in reference health facilities, as well as the organization of referral and contra-referral strategies.
• Where requested, WHO will assist in securing additional international clinical management capacity.

In countries that share a border with a country experiencing a yellow fever outbreak, and in all other countries where yellow fever is endemic

• Clinical management standards should be reiterated to all health practitioners.
• Care/supportive treatments for patients with suspected and confirmed yellow fever should be made available free of charge.
• Insecticide-impregnated mosquito nets should be provided in clinical settings and for people who rest during the day (pregnant women, infants, sick or bedridden individuals), especially in countries neighboring those currently experiencing epidemics. Malaria and dengue rapid detection tests should be made available to support differential diagnosis.

All other countries

• All countries may be at risk of importation through international travel and trade. Those with infestation by Aedes spp. mosquitoes are further at risk of local transmission. Therefore all countries should be ready to detect cases of yellow fever and to transfer patients with suspected yellow fever (either from country entry point or from health facility of first admission) to pre-identified infectious disease health units competent to manage yellow fever cases. The WHO yellow fever vaccination recommendations for travelers should be enforced, and travelers returning from countries affected by yellow fever informed to report to the health authorities in case of a febrile event with suspected signs within a week from return, especially if the patient had not been vaccination against yellow fever prior to travel to or through an affected country or area.

Social mobilization and risk communication

Populations need and have a right to information about yellow fever (including symptoms, mode of transmission, need for vaccination, possible adverse effect following immunization, the need to seek medical care early, and other personal and environmental protective strategies) adapted to local contexts, providing realistic recommendations, and translated into local languages. Access to essential care, supplies, and advice should be ensured. It is essential to engage community influencers, and to implement mechanisms to identify and address misinformation and rumors. Community mobilisation approaches for engagement in surveillance and vector control should be adopted, and efforts made to sustain the effects beyond the period of the vaccination campaign especially in the border areas.

Risk-communication strategies should be based on an analysis of socio-cultural barriers to adopting interventions (e.g. vaccine hesitancy or refusal, vector control, seeking medical care) and on consultations with the communities. They should segment audiences, clearly define results and activities for each of them, and set the monitoring and evaluation framework, process and tools. Preferably, operational research utilizing rapid qualitative and Knowledge, Attitude and Practice (KAP) surveys should be implemented to support work to understand barriers to applying interventions.
especially prior to mass vaccination campaigns, but should not delay intervention.

WHO, UNICEF and key operational partners should coordinate their messages and, wherever possible, activities for greater effect and consistency. Evidence-based risk communication can build confidence and trust in yellow fever vaccination and the health system in case any accident or adverse event occurs during mass vaccination. Depending on the country context, messages may address various issues, from disease presentation to the vaccination to travelers.

In countries experiencing an outbreak
- If they do not exist, health authorities should set up mechanisms to communicate risk and mobilise society, and continuously assess the effectiveness of community engagement strategies, focusing on analysing public concerns and knowledge gaps with regards to the on-going outbreak, and on sound monitoring of both implementation and results.
- Micro-plans should integrate risk communication and social mobilisation activities at local level. Activities should target groups most affected and most at risk.
- The approaches for different contexts (urban, peri-urban, and rural) will differ due to population density, infrastructure, work and daily routines, and access to services, communications and media. This should be documented and incorporated into micro-planning and wider coordination.
- Communication materials should be adapted to local cultural perceptions and languages, and community health workers, mobilisers, volunteers and health workers should be trained on key messages and, if needed, on interpersonal communication skills.
- Supervision of and reporting by actors engaged in risk communication activities should be ensured.
- Partners should facilitate the development and implementation of community-led action plans and community monitoring mechanisms, in priority areas at a minimum, and not limited to the period of the vaccination campaign.
- Vector-control communication should engage communities, families and individuals through health education and social mobilization informed by KAP assessment to tailor strategies and messages.

- Vaccine and vaccination campaigns messages should be based whenever possible on the results of KAP surveys, focus group discussions, and rumor monitoring to identify and address vaccine hesitancy. Key stakeholders include communities, families and individuals, influential individuals, community leaders, community based organizations (CBOs), religious groups, civil society organizations (CSOs) and professional groups, services providers and local authorities.

In countries that share a border with a country experiencing a yellow fever outbreak, and in all other countries where yellow fever is endemic
- Preparedness plans and materials used for social mobilization should be reviewed urgently, especially in countries neighbouring those experiencing an outbreak.
- Information should be made available to communities at each entry point in the country in local language(s), and should address clinical presentation, health seeking behavior, and the need for travellers to be vaccinated.

All other countries
- Authorities should assess the pertinence of developing contingency plans and ensure that information is made available at main entry points at a minimum.
- Travelers to affected countries should be made aware of the compulsory requirement for vaccination at least 10 days prior to departure.
- Travelers returning from affected countries should be informed of how to recognize signs and symptoms, the importance of case notification and how to seek treatment in case of suspected infection.

Vector control

The yellow fever virus is transmitted to humans by Aedes species mosquitoes that also spread dengue, Chikungunya and Zika viruses. The implementation of vector control measures and the prioritization of interventions in the case of a yellow fever outbreak should follow the guidance set out in the WHO guidance document Vector control operations framework for Zika, which will be published shortly.
Well-implemented vector control can effectively reduce the transmission of vector-borne diseases if significant resources are available and communities fully engaged. Vector control is a cross sectoral approach requiring the investment and coordination of several ministries (e.g. health, sanitation and environment, education). WHO and partners will support efforts to intensify existing national Aedes mosquito vector surveillance and control programs, especially for Aedes spp., and improve access to larvicides and monitor insecticide resistance in countries with an ongoing outbreak.

Countries can be categorized on the basis of their entomological situation as follows:

A: Ongoing yellow fever outbreak AND Aedes present AND intense yellow fever transmission in humans

B: Neighbouring a country with an ongoing outbreak AND Aedes present AND limited yellow fever transmission in humans (a small number of imported or autochthonous cases reported)

C: Other country AND Aedes present NO YF human transmission

Different targeted interventions are recommended depending on which category a country falls in (table three), but in all countries, community mobilization should start to eliminate/cover urban and peri-urban standing water mosquito breeding sites around homesteads.

Countries in categories A and B

- Vector-control measures should come as a package, addressing the control of adult mosquitoes and larvae, the removal of eggs, and the prevention of mosquito bites through personal protection. Personal protection methods are advised for patients who are being treated for yellow fever and for members of affected communities.
- Targeted residual spraying is the primary vector-control intervention for immediate response. During outbreaks of vector borne diseases authorities should implement space spraying to kill adult vectors so as to reduce virus transmission. An appropriate WHOPES-recommended insecticide should be selected, 17, 18
- Control measures to target breeding sites should be immediately intensified, especially when an outbreak occurs in urban areas. These control measures must be complemented with long-term monitoring of mosquito population density.

Countries in category C

- WHO and partners will support governments to play a direct and pre-emptive role in implementing vector surveillance and vector control at the scale needed to prevent transmission. To be most effective, action must be taken before human cases of yellow fever occur.

Vector-control activities should be guided by an assessment of population immunity, vaccination coverage, mosquito density, and access to care and to control measures.

http://www.who.int/whopes/Space_Spray_products_February_2016.pdf (last accessed 23 May 2016.)

18 WHOPES-recommended compounds and formulation for control of mosquito larvae:
http://www.who.int/whopes/Mosquito_larvicides_Feb_2016.pdf (Last accessed 23 May 2016.)

17 WHO. Recommended insecticides for space spraying against mosquitoes.
Table 3 | Recommended yellow fever response interventions by country classification

<table>
<thead>
<tr>
<th>Country Classification</th>
<th>Intensification of entomological surveillance, assessing the density of Aedes mosquitoes around residences of detected cases (400 m radius), yellow fever patient treatment sites, and in areas where there is known to be a high risk of mosquito proliferation.</th>
<th>Monitoring of ports of entry</th>
<th>Monitoring of insecticide resistance of Aedes mosquitoes where insecticide-based interventions are being used or planned</th>
<th>Monitoring and evaluation of the quality and impact of control measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neighbouring epidemic AND Aedes present AND limited human transmission of yellow fever*</td>
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<tr>
<td>Other country AND Aedes present AND no human transmission of yellow fever</td>
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</tbody>
</table>

**Vector surveillance and risk assessment**

**Vector control**

Adaptation of vector control strategies to the intensity of virus transmission and to the timing of the mosquito breeding season, including source reduction

Provision of insecticide-impregnated mosquito nets as part of the management of suspected yellow fever cases, and where needed, to affected communities

Distribution and appropriate use of mosquito repellents

Implementation of vector control measures integrated with surveillance

Conduct adult vector control, including indoor space spraying in identified hot spots

Application of larvicides in targeted areas not amenable to source reduction

**Specific social mobilization interventions**

Community mobilization with source reduction

Risk communication and promotion of personal protection

*Few imported or autochthonous cases reported.
RESPONSE

COORDINATION

An effective response depends on effective national and international coordination. WHO will continue to keep member states informed through IHR focal points and in its public communications, and to mobilize technical experts through the Global Outbreak Alert and Response Network. WHO will also support the mobilization of other resources (financial, logistical or other), in addition to the resources being provided bi-laterally by other partners or through a health sector/cluster coordination mechanism.

In countries experiencing an outbreak

- WHO and partners will support national and local health authorities to continue leading the coordination of all stakeholders. The national coordination mechanism should include an appropriate structure and management, and a framework for the collection of information, decision making, and for action implementation. Leadership should also design and implement a framework for response monitoring so as to adapt interventions to the evolving situation.
- Intersectoral collaboration at governmental level is recommended to help mobilize national and local ministries involved in health, environmental health, and in education, social development and tourism sectors, communication sectors, and entry points (ports, airports, ground entry points). Public practitioners and community health workers, private practitioners and traditional healers must all be engaged in response and prevention activities. In parallel, local, national, and international partners, non-governmental organizations (NGOs), the donor community, community leaders and private entities should be encouraged to engage in response and prevention interventions.
- Domain-specific working groups within the wider national and subnational coordination mechanisms (e.g., a risk communication and social mobilization sub-group) should be established.
- Cross-border coordination with surrounding countries at risk should be established.
- WHO and partners should be ready to mobilize self-sufficient multidisciplinary and ready-to-operate teams (epidemiologists; public and media communication officers; social mobilization and community engagement officers; logistician, laboratories, case management vector control, administration staffs) for large-scale assistance.

In countries that share a border with a country experiencing a yellow fever outbreak, and in all other countries where yellow fever is endemic

- National and sub-national coordination capacity should be reviewed as soon as possible.
- Health authorities should be familiar with the ICG procedures and criteria for the deployment of vaccines from the global emergency stockpile and the related ICG vaccine request forms.
- A coordination structure or disease taskforce should be created to coordinate and/or conduct risk assessments, prepare and plan on the basis of those assessments, and convene partners to assess needs and mobilise resources. Health authorities should be familiar with the response capacity of the main external health actors present in country (e.g., NGOs, donors, presence or not of the Cluster system of the Inter-Agency Standing committee, and UN agencies), and have defined how the response to an outbreak would be coordinated (who is doing what, lines of reporting, roles and responsibilities.

All other countries

- National and local health authorities should review coordination mechanisms, and assess the risk of an outbreak in case of a yellow fever importation.
### Table 4: Global yellow fever response monitoring indicators (priority indicators in bold)

<table>
<thead>
<tr>
<th>Domain</th>
<th>Activity</th>
<th>Indicator</th>
<th>Target</th>
<th>Information source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccination</td>
<td>Availability of vaccines for urban outbreaks</td>
<td>% of request of vaccine supply complying with ICG criteria responded to within 1 week</td>
<td>100%</td>
<td>ICG activity report</td>
</tr>
<tr>
<td></td>
<td>Monitoring of adverse event following immunization (AEFI) with yellow fever vaccine</td>
<td>% of mass vaccination campaigns where active and passive daily AEFI monitoring is being carried out</td>
<td>100%</td>
<td>National reports to the ICG, reports from responsible entity/agency</td>
</tr>
<tr>
<td></td>
<td><strong>Global level surveillance</strong></td>
<td><strong>Weekly number of new countries reporting yellow fever cases</strong></td>
<td>🔄</td>
<td>Surveillance reports</td>
</tr>
<tr>
<td></td>
<td><strong>Health Security and International Health Regulation</strong></td>
<td><strong>Weekly number of new epidemic countries</strong></td>
<td>🔄</td>
<td>Surveillance reports</td>
</tr>
<tr>
<td></td>
<td>Specimen shipment and processing</td>
<td>% of affected countries complying with the IHR obligations for notification</td>
<td>100%</td>
<td>IHR reports</td>
</tr>
<tr>
<td></td>
<td></td>
<td>% of countries carrying out entry screening for yellow fever vaccination proof, on main entry points, on travelers coming from epidemic countries</td>
<td>100%</td>
<td>Situation reports</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Weekly number travelers reported not carrying a valid yellow fever vaccination card while entering country, per epidemic country, and in total</td>
<td>0%</td>
<td>Situation reports</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Weekly number of travelers vaccinated upon entry to country, per epidemic country, and in total</td>
<td>0%</td>
<td>Situation reports</td>
</tr>
<tr>
<td></td>
<td><strong>Vector control</strong></td>
<td><strong>Weekly number of new priority areas identified for vector control per country</strong></td>
<td>🔄</td>
<td>Surveillance, situation and other reports</td>
</tr>
<tr>
<td></td>
<td><strong>Case management</strong></td>
<td><strong>% of affected countries having disseminated an appropriate case definition</strong></td>
<td>100%</td>
<td>Assessment</td>
</tr>
<tr>
<td></td>
<td><strong>Risk communication and social mobilization</strong></td>
<td><strong>% of countries with updated risk communication/social mobilization strategies/plans</strong></td>
<td>100%</td>
<td>Situation and other reports</td>
</tr>
<tr>
<td></td>
<td>International coordination</td>
<td>% of epidemic countries and neighboring countries where risk communication and community engagement material is available in appropriate international and local languages at main official points of entry/exit</td>
<td>100%</td>
<td>Assessment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>% of epidemic countries with national coordination frameworks and response plans in affected areas</td>
<td>100%</td>
<td>WHO situation up dates</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Number and list of partners supporting YF national response per domain (surveillance, vaccination, cases management, vector control, social mobilization, coordination) per country and globally</td>
<td>100%</td>
<td>WHO situation up dates</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total number of international technical experts deployed by week from GOARN partners</td>
<td>Country specific</td>
<td>4Ws, countries reports, WHO situation reports, Health sector/cluster reports</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Total number of WHO staff by week supporting the response at sub-national, national and international levels</td>
<td>Country specific</td>
<td>WHO situation up dates</td>
</tr>
</tbody>
</table>

*Any country reporting yellow fever cases, including sporadic sylvatic cases. †See International Health Regulation (2015) Third edition; Part II information and public health response; Article 6 Notification.*
Rationale for response monitoring

Effective response operations depend on continuous, regular and detailed surveillance and response monitoring, analysis and reporting. Surveillance and response monitoring data and analysis provide an overview of trends, and are used to adjust needs, targets and funding requirements. Response monitoring data and analysis also enable leadership to review the progress of the overall response and make adjustments where necessary.

WHO is working to provide Member States with recommendations on strengthening surveillance and reporting systems in the context of current yellow fever outbreaks. WHO also encourages and requests partners to regularly report on their response activities at the global, regional and national levels through an online portal currently in development.

The overall yellow fever response strategy is being continually reassessed to respond to changing circumstances. WHO publishes a global situation report on a weekly basis through the WHO website.

### SUMMARY OF REQUIREMENTS

**REQUIREMENTS (US$)**

**94.14 M**

WHO is currently working with all partners to consolidate needs and requirements across the response based on the strategic response framework. The budget requirements identified to date by WHO are summarized below (table five).

WHO headquarters, the WHO regional office for Africa, and the relevant country offices have a consolidated requirement of **US$ 94,143,426** (annex B). For all activities conducted by WHO there is a total need of approximately **US$ 80.31 million**. There is a total request of approximately **US$ 13.82 million** for human resources. There is a total partner requirement of **US$ 11.72 million** (annex B) on behalf of those partners who have informed WHO of their needs so far. Most activities are taking place either in, or in support of, the African regional office and affected countries.

Response activities and related human resource requirements across all levels have been aligned to the four strategic objectives of this response framework.

To support the ongoing response, existing funds have been matched against some requirements for Yellow Fever activities:

- **US$ 3 200 000** from ICG revolving fund for procurement of YF vaccine
- **US$ 500 000** from USAID for Angola outbreak and response activities
- **US$ 2 200 000** from Contingency Fund for Emergencies, which will need to be reimbursed to the CFE

Additionally other funding to support vaccination activities in Angola, DRC and Uganda

WHO is also working on a model to examine budget estimates for epidemic preparedness in at-risk countries/locations neighbouring currently affected countries. Based on ongoing preparedness work, usual costs are between US$ 2.5 and four million per country for a hazard-specific preparedness and response contingency plan, and around US$ 10 million for an annual all-hazard preparedness plan (which ranges from US$ six to 15 million in the African region). Of the yellow fever affected and surrounding countries, only Uganda, DRC, and Tanzania currently have ongoing preparedness programmes in place.
PART II: JOINT OPERATIONS PLAN

JOINT OPERATIONS PLAN

STRATEGIC OBJECTIVE 1 - End outbreaks in currently affected countries through targeted vaccination and other public health measures

STRATEGIC OBJECTIVE 2 - Prevent morbidity and reduce mortality through early case detection and strengthened case management

STRATEGIC OBJECTIVE 3 - Prevent international spread

STRATEGIC OBJECTIVE 4 - Prioritize research to improve access to yellow fever vaccine, and to improve the effectiveness of other prevention and control interventions
STRATEGIC OBJECTIVE 1

End outbreaks in currently affected countries through targeted vaccination and other public health measures

Vaccination (reactive and pre-emptive)

Mass vaccination campaigns are critical in the control of a yellow fever epidemic. The earlier a mass vaccination campaign begins, the more will cases of disease be prevented. Vaccination has been initiated in the affected countries with varying coverage ranging from 30% to 96% in Angola and Uganda respectively. However, many at risk districts and provinces require urgent vaccination to create a sufficient cordon sanitaire around areas reporting locally transmitted cases. When all high risk areas have been covered by the vaccination campaign and subject to availability of vaccines, vaccination will be expanded outward into adjacent areas, to include all areas at risk. If vaccines and resources are limited, vaccination will be targeted to the age groups with the highest attack rates i.e. ages 6 months to 45 years.

Due to emerging concerns about the spread northwards through Angola to DRC, and the potential impact this may have on large urban centres, a large scale vaccination campaign will be carried out in late July and August 2016 in areas that pose the greatest risk. The identification of risks, target populations and areas is being informed by current disease epidemiology, and modelling to determine risk levels:

1. A 75-100km belt spanning the border between Angola and DRC
2. Other high risk in-land areas associated with local mining areas, and big markets attracting large migrant populations and population movements to and from Angola
3. Vaccination of at risk populations around confirmed cases of local transmission and a phased pre-emptive vaccination of the entire population of Kinshasa to mitigate further spread within and internationally.

According to vaccine supply and emerging priorities it will also be assessed further whether there are communities outside the proposed 100km belt that should be factored into the pre-emptive campaign in order to prevent further spread of the disease. As areas are vaccinated the coordinated recording of coverage will be documented accurately and shared appropriately to inform ongoing planning.

The unit cost of implementing such a campaign is approximately two US dollars per vaccine administered, which is inclusive of all costs, broken down into approximately one dollar for the vaccine itself and one dollar for the operational costs of vaccine delivery.

As DRC is GAVI eligible, and pre-emptive vaccination campaigns are funded through this mechanism during an emergency, these costs will be covered through the existing GAVI mechanism. However, the cost per vaccine provided by GAVI is 25 cents per vaccine for operational cost, and allowing for the increased cost of delivering vaccinations in a complex urban environment such as Kinshasa, one dollar per vaccine administered will need to be raised for DRC.

Angola is not covered by GAVI, but the Angolan Government has committed to funding half the vaccination costs during the current outbreak. Therefore one dollar for each vaccine administered will need to be raised for Angola.

In view of this strategic re-orientation there is a need to scale up the human resources for each country and for the WHO Africa Regional Office to facilitate robust micro-planning and logistical preparation required to deliver such a vaccination programme. The human resource cost for implementing this can be found within the section relating to strategic objective three below.

There are limited vaccine stocks immediately available for the pre-emptive campaign, and therefore prioritization will be required in the micro-planning, along with synchronising the approach between DRC and Angola, and trying to achieve the vaccinations in as short a time as is realistic and as vaccine supplies with associated logistics allow.
WHO recommends the use of dose fractioning of the vaccine in order to get greater coverage from the limited stock available. Practical issues that need further consideration include sourcing of appropriate syringes, ensuring reconstituted vials are kept cool (4-8 °C) and used within six hours of opening, training of health workers on vaccine reconstitution/use and developing messages on the new approach to ensure community acceptance. Dose sparing would be more challenging in rural areas, and cannot be performed in children under two years old. Lastly, there are slightly different recommendations for the product of each vaccine manufacturer which need to be taken into account for any dose sparing strategy.

**Vaccination across the border of Angola and DRC**

In collaboration with Imperial College of London and the University of Oxford-KEMRI Wellcome Trust Programme, the WHO and partners have used the available data on incidence, recent vaccination activities, vector distribution, past occurrence of yellow fever and population movement patterns to model the risk of spread and help identify areas to target the available vaccine resources on the border of Angola and DRC.  

It is proposed to vaccinate the higher risk districts falling inside this 100km corridor, using the risk scores to prioritize which districts should be targeted first. Within this approach there are two courses of action possible. The first will be to vaccinate the entire population, while the second will be to vaccinate only the urban population within each district. Regional and country experts advise that the minimum functional unit for vaccination is the district.

Due to the logistical challenges involved in rural areas, dose fractioning would not be proposed in this area. WHO would recommend using full doses of yellow fever vaccine in these settings.

**Figure 2 | Map of border districts targeted for full dose campaign**

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Targeting Kinshasa City

Population estimates vary significantly, but the total population requiring vaccination for the purposes of this plan is approximately eight million. However, the planned number for vaccination is approximately 10 million, in order to take account of the difficulties in estimating population and projected wastage of vaccines. WHO recommends considering dose fractioning as a way to extend the limited stock of vaccine to cover the entire city in a phased approach. This method would be more feasible in an urban setting than in a remote rural area.

Figure 3 | Map of Kinshasa City (DR Congo) targeted for fractionated dose

Table 4 | Target population for the pre-emptive vaccination campaign

<table>
<thead>
<tr>
<th>Country</th>
<th>Border Area</th>
<th>Other Area</th>
<th>Overall Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angola</td>
<td>1,307,977</td>
<td>3,083,654</td>
<td>4,391,631</td>
</tr>
<tr>
<td>DRC</td>
<td>2,998,015</td>
<td>8,053,536</td>
<td>11,041,551</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>15,433,182</td>
</tr>
</tbody>
</table>

Table 5 | Total requirements for the vaccination campaign

<table>
<thead>
<tr>
<th>Component</th>
<th>Requirement</th>
<th>Quantity</th>
<th>Unit Cost (USD)</th>
<th>Shipping Cost</th>
<th>Total Cost (USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fractionated</td>
<td>Vaccine</td>
<td>2,500,000</td>
<td>1</td>
<td>50,000</td>
<td>2,550,000</td>
</tr>
<tr>
<td>Fractionated</td>
<td>Syringes</td>
<td>10,000,000</td>
<td>0.06</td>
<td>700,000</td>
<td>1,300,000</td>
</tr>
<tr>
<td>Fractionated</td>
<td>Operational Cost</td>
<td>10,000,000</td>
<td>1.25</td>
<td></td>
<td>12,500,000</td>
</tr>
<tr>
<td>Fractionated</td>
<td>Technical Support</td>
<td>50,000</td>
<td>4</td>
<td></td>
<td>200,000</td>
</tr>
<tr>
<td>Full Dose</td>
<td>Vaccine</td>
<td>7,883,051</td>
<td>1</td>
<td>50,000</td>
<td>7,933,051</td>
</tr>
<tr>
<td>Full Dose</td>
<td>Syringes</td>
<td>7,883,051</td>
<td>0.1</td>
<td>700,000</td>
<td>1,488,305</td>
</tr>
<tr>
<td>Full Dose</td>
<td>Operational Cost</td>
<td>7,883,051</td>
<td>1</td>
<td></td>
<td>7,883,051</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>33,854,407</td>
</tr>
</tbody>
</table>
Table 6 | Total requirements for the vaccination campaign by country

<table>
<thead>
<tr>
<th>Requirement</th>
<th>DRC Kinshasa</th>
<th>DRC Border &amp; &lt;2s Kinshasa</th>
<th>Angola</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doses</td>
<td>10,000,000</td>
<td>3,315,755</td>
<td>4,567,296</td>
</tr>
<tr>
<td>Vaccine</td>
<td>2,500,000 (fractionated)</td>
<td>3,315,755</td>
<td>4,567,296</td>
</tr>
<tr>
<td>Syringes</td>
<td>10,000,000</td>
<td>3,315,755</td>
<td>4,567,296</td>
</tr>
<tr>
<td></td>
<td>0.1 ml syringes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Operational Cost</td>
<td>12,500,000 USD</td>
<td>3,315,755 USD</td>
<td>4,567,296 USD</td>
</tr>
<tr>
<td>Technical Support</td>
<td>200,000 USD</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Key Assumptions

- Fractionated dosing is possible in urban centres not rural
- Fractionated dosing not possible in under two year olds in Kinshasa (n=200,211)
- Vaccine from Brazil only option for fractionated dosing currently
- Wastage of four percent needs to be factored in for all areas other than Kinshasa, where MoH DRC have already built in wastage
- Fractionated dose – five doses from each vial, including wastage reduces to four
- Technical support includes Risk Communications, Research, Monitoring & Evaluation and Programmatic Work, for the fractionated dosing in Kinshasa
- Operational cost 1.25 US $ for Kinshasa, one US $ USD all other areas

At the time of writing the total number of vaccines instock is approximately four million, with an expected 13 million by the end of July due to an increase in production. If a decision is made to use dose fractioning, both the cross-border belt approach and the Kinshasa approach could be done simultaneously, phasing each by priority geographies, with the suggested timing for the campaign being late July to mid-August.

Implementation of a dose-fractioning strategy would require more resources and logistics in terms of appropriate syringes and cold chain, including training and close monitoring of the campaigns. Organizations will work in collaboratively with the Ministries of Health of the affected countries to link with and support existing vaccination campaigns.

The human resource costs for implementing this vaccination plan are stipulated under strategic objective three below.
<table>
<thead>
<tr>
<th>Key Activity</th>
<th>Location</th>
<th>Partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccination campaign and post campaign evaluation</td>
<td>DRC</td>
<td>Save the Children, MoH, WHO, UNICEF, MSF</td>
</tr>
<tr>
<td>Preparedness and deployment readiness of Emergency Health Team for all at risk areas but priority for support</td>
<td>DRC</td>
<td>Medair</td>
</tr>
<tr>
<td>Vaccination of cross-border travellers, migrant workers and host communities</td>
<td>Angola and DRC border</td>
<td>IOM</td>
</tr>
<tr>
<td>Financing the global yellow fever vaccine emergency stockpile and contributing to operational cost for vaccination campaigns</td>
<td>Global</td>
<td>GAVI</td>
</tr>
<tr>
<td>Ensuring all newly arriving refugees are included in respective national screening and vaccination programs/ strategies</td>
<td>Kenya, Rwanda, Tanzania, Uganda, DRC and others</td>
<td>UNHCR</td>
</tr>
<tr>
<td>Design and support of post-campaign independent monitoring</td>
<td>Angola</td>
<td>US-CDC</td>
</tr>
<tr>
<td>Provide technical support to the National Directorate of Public Health in the preparation and implementation of the current response to extend the vaccination campaign to all districts in Luanda and to other provinces in the country, focusing on the coordination of the response, and strategic and operations planning.</td>
<td>Angola</td>
<td>UNDP, MoH</td>
</tr>
<tr>
<td>Provide logistical support to the vaccination efforts</td>
<td>Lunabda, Angola</td>
<td>UNFPA Angola</td>
</tr>
<tr>
<td>Support vaccination micro-planning for efficient use of vaccine and monitor campaign coverage. Providing additional in-country capacity support for vaccine management and coordination</td>
<td>Angola</td>
<td>UNICEF EASRO</td>
</tr>
<tr>
<td>National Immunization campaign for all population</td>
<td>Sao Tome</td>
<td>UNICEF EASRO</td>
</tr>
<tr>
<td>Advocacy, training and community sensitization for reactive vaccination campaign.</td>
<td>Gabon</td>
<td>UNICEF Gabon</td>
</tr>
<tr>
<td>Reinforcement of the routine immunization system through the purchase of VAA vaccine and consumables, the social mobilization, the coordination and the surveillance and risk assessment in collaboration WHO</td>
<td>Gabon</td>
<td>UNICEF Gabon</td>
</tr>
<tr>
<td>Support YF pre-emptive campaigns operations and monitoring</td>
<td>Angola</td>
<td>UNICEF EASRO, Angola, MoH, WHO</td>
</tr>
</tbody>
</table>
Risk Communication and Community Engagement

When a yellow fever epidemic has been declared, there is likely to be widespread public concern and media attention. Therefore, efforts to reach communities with key messages about the outbreak have to be instituted and sustained throughout the epidemic.

The strategy will support the deployment of social scientists including anthropologists to explore local beliefs about disease transmission and conduct operational research to understand barriers. Knowledge, Attitude and Practice (KAP) surveys will be conducted to measure the understanding and application of this key information.

This will allow the messages to be culturally relevant, to be communicated through channels which maximize their impact and will assist in dispelling misconceptions. It will be critical for media campaigns to be conducted in multiple local languages to maximize the reach they have. Multiple channels will also be key in ensuring the reach and impact of the messaging; including national and international media, television, leaflets, social media, and the development of an Android/iOS phone application. Activities mobilizing community organizations and networks will include training community workers in inter-personal communication for yellow fever prevention, as well as dynamic and interactive community-based approaches in high risk villages. Outreach to the public will prioritize evidence based channels such as: meetings with the community, religious and political leaders, presentations at markets, health centres, schools, religious centres and house-to-house visits.

Together these risk communication and community engagement methods will aim to both raise general awareness, whilst also providing specific, clear information on:

1. Why they should be vaccinated
2. When and where to go for vaccination
3. Why it is important for travellers to present a valid yellow fever vaccination card at borders and points of entry
4. When and where to seek medical attention;
5. How yellow fever is spread; and
6. How to reduce mosquitoes and their breeding sites.

In any setting where dose fractioning is considered, community engagement and risk communication will be very important in order to gain health worker and community acceptance. People will need to be informed that fractional dosing does not mean partial efficacy or an inferior vaccine.
Table 8 | Partner Activities - Risk Communication and Community Engagement

<table>
<thead>
<tr>
<th>Key Activity</th>
<th>Location</th>
<th>Partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social mobilization in support of vaccination campaign and vector control activities</td>
<td>Angola, DRC and Uganda</td>
<td>IFRC</td>
</tr>
<tr>
<td>Community engagement through information, education and communication (IEC) channels for raising awareness on vaccination campaign</td>
<td>Angola</td>
<td>World Vision International, MOH, WHO, UNICEF, CDC and MSF (Spain)</td>
</tr>
<tr>
<td>Providing information to asylum seekers at entry points and refugee hosting sites in local language(s), on clinical presentation, health seeking behaviour, and the need for vaccination. Training community workers in inter-personal communication on yellow fever</td>
<td>Kenya, Rwanda, Tanzania, Uganda, DRC, others</td>
<td>UNHCR</td>
</tr>
<tr>
<td>Development and implementation of communication strategy targeting cross-border travellers, migrant workers and host communities including border community engagement and peer support for migrant worker</td>
<td>Angola and DRC - border areas</td>
<td>IOM</td>
</tr>
<tr>
<td>Community sensitization</td>
<td>DRC</td>
<td>Malteser International</td>
</tr>
<tr>
<td>Provide technical support to CO on YF social mobilization and risk communication and support the development of an integrated communication response including the effective use of available and existing community communication platforms</td>
<td>Uganda, Namibia, Zambia</td>
<td>UNICEF ESARO, MOH, WHO</td>
</tr>
<tr>
<td>UNICEF ESARO C4D team to provide technical support to Angola CO. Mapping of and re-activating the polio communication structure and mobilization of Red Cross volunteer in areas of vaccination campaign</td>
<td>Angola</td>
<td>UNICEF ESARO, Angola Red, WHO, CDC</td>
</tr>
<tr>
<td>Development of risk communication strategies, mobilization of community networks, media campaign and production of culturally relevant communication materials</td>
<td>Western and Southern African region, DR Congo, Sao Tome</td>
<td>UNICEF WSARO</td>
</tr>
<tr>
<td>Technical assistance to countries for embedding risk communication, community engagement and crisis communication in country preparedness and response plans according to the global SRF. Technical assistance to develop/update operational tools and to reinforce YF messaging in regular RI communication activities</td>
<td>Cape Vert, Congo, Gabon, Sao Tome</td>
<td>UNICEF WSARO</td>
</tr>
<tr>
<td>Providing technical support to develop regional risk communication and community engagement approach for prevention of yellow fever</td>
<td>Global</td>
<td>UNICEF HQ</td>
</tr>
</tbody>
</table>

Vector Control

Eliminating adult and larval mosquito populations and potential mosquito breeding sites reduces the vector that transmits yellow fever. Mosquito control efforts are most effective when the major vector is a peri-domestic mosquito such as Aedes Aegypti. In such cases, both the management of individual homes (using insecticide sprays and protecting water containers) and community-based programs can have substantial impact on the size of infected mosquito populations.

Significant resource will be allocated to integrated vector control as part of this strategy, and in addition countries will be provided technical support in vector control activities, including WASH expertise. A number of entomologists will be deployed and vector control field assessments will be supported in high risk areas. Communities will also be supported to use mosquito nets, especially on the beds of ill patients. Consequently, the scale up plan below has costed the HR needs to deploy vector control experts in the provinces and the districts.
### Table 9 | Partner Activities - Vector Control

<table>
<thead>
<tr>
<th>Key Activity</th>
<th>Location</th>
<th>Partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contribution from the WASH section specialists regarding vector control</td>
<td>Western and Southern African region</td>
<td>UNICEF WCARO</td>
</tr>
<tr>
<td>Develop guidance on vector control activities for UNICEF and provide technical support to UNICEF country offices on vector control activities for prevention of yellow fever</td>
<td>Global</td>
<td>UNICEF HQ</td>
</tr>
<tr>
<td>Community based vector control</td>
<td>Angola, DRC</td>
<td>IFRC</td>
</tr>
</tbody>
</table>
STRATEGIC OBJECTIVE 2

Prevent morbidity and reduce mortality through early case detection and strengthened case management

Surveillance & Risk Assessment

Coordinating the collection, analysis and dissemination or communication of vital information is critical in early case detection and in strengthening case management. Assessing the health risks, the needs, the response of the sector and the identified gaps will also be key in allocating resources appropriately to prevent morbidity and reduce mortality. Diagnosis and reporting of new cases will be based on standard case definitions and laboratory confirmation, and risk assessment requires comprehensive investigation of all confirmed cases informing the basis of timely vaccine allocation and the implementation of vaccination campaigns. The standard case definitions will be widely disseminated. All health facilities will be required to send daily and weekly reports on the number of cases and deaths. All districts will prepare summary reports of health facility data and submit them to the provincial level.

These reports will include: the period of time covered by the report, the number of health facilities that reported (including the health facilities that reported no cases of suspected yellow fever), the total number of health facilities in the district, the total number of suspected yellow fever cases and deaths during the reporting period and the number of vaccinations planned and the number given.

Such reports will be consolidated by developing and maintaining a global laboratory and enhanced epidemiological database to allow the appropriate monitoring, tracking, verification and mapping of yellow fever.

Risk mapping and specific field risk assessments will also be conducted in high risk areas to guide further response planning.

It will be important to strengthen surveillance at the provincial level to ensure completeness and quality of reporting. Support in case investigations, case classification and in assessment of surveillance quality at the provincial level will be prioritized to improve the early detection, reporting and referral of suspected cases through active surveillance and investigation.

The strengthening of disease surveillance in the city of Kinshasa and Kongo Central Province in the Democratic Republic of Congo is seen as a priority and will be supported through: investigation of mission alerts; strengthening the capacity of laboratories; conducting active research; and through logistics training.

Laboratory capacity and capacity for specimen collection, packaging and shipment for confirmation are important components of surveillance and risk assessment. The laboratory capacity should also include the ability to rule out or determine co-infections, including differential diagnosis for negative cases meeting suspect case definition for Yellow Fever. For maximizing testing capacity, the option of deploying mobile laboratories is also being explored.

WHO will coordinate updates on epidemiology and on laboratory results and will conduct modelling on yellow fever risk and a global risk assessment.
### Table 10 | Partner Activities - Surveillance & Risk Assessment

<table>
<thead>
<tr>
<th>Key Activity</th>
<th>Location</th>
<th>Partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community based surveillance</td>
<td>Angola, DRC (potentially surrounding countries, Namibia, Zambia)</td>
<td>IFRC</td>
</tr>
<tr>
<td>Epidemiological surveillance</td>
<td>DRC</td>
<td>IMC</td>
</tr>
<tr>
<td>Surveillance through community health workers and clinics in Medair supported areas</td>
<td>Eastern DRC</td>
<td>Medair</td>
</tr>
<tr>
<td>Providing guidance on the preparedness plan</td>
<td>DRC</td>
<td>Malteser International</td>
</tr>
<tr>
<td>Health screening of cross border travelers and host communities at priority ground crossings and mobility hotspots at the border spaces of Angola and DRC</td>
<td>Angola and DRC - border areas</td>
<td>IOM</td>
</tr>
<tr>
<td>Mission to assess the situation of the outbreak</td>
<td>Angola</td>
<td>ECDC</td>
</tr>
<tr>
<td>Preparing risk assessments and epi updates, RT report and weekly CDTR, Daily screening for the round table – International health regulations</td>
<td>ECDC-Stockholm Sweden</td>
<td>ECDC</td>
</tr>
<tr>
<td>Strengthening of surveillance at province level, completeness of and quality of reporting, case investigations, case classification; assessment of surveillance quality and AEFI Surveillance</td>
<td>Angola</td>
<td>US-CDC</td>
</tr>
<tr>
<td>in-country Lab services: PCR, IgM, Test evaluation; Confirmatory test and genotyping</td>
<td>Angola, US</td>
<td>US-CDC</td>
</tr>
<tr>
<td>Continued surveillance and risk assessment activities at entry points and in refugee hosting sites in coordination with national authorities and partners</td>
<td>Kenya, Rwanda, Tanzania, Uganda, DRC, others</td>
<td>UNHCR</td>
</tr>
<tr>
<td>Providing laboratory manpower and supplies for serology and molecular detection of yellow fever virus diagnostics</td>
<td>DR Congo</td>
<td>IPD</td>
</tr>
<tr>
<td>Monitoring, evaluation and documentation of communication activities (supervisions, SMS, documentation)</td>
<td>DR Congo</td>
<td>UNICEF WCARO, MoH and Ministry of Communication and Media</td>
</tr>
<tr>
<td>Support to IELE (national Agency in charge of epidemiological surveillance) through the training of district level Focal Points on case investigation and case management</td>
<td>Gabon</td>
<td>UNICEF WCARO, MoH</td>
</tr>
<tr>
<td>Nationwide campaign on supervision</td>
<td>Gabon</td>
<td>UNICEF WCARO, MoH</td>
</tr>
<tr>
<td>Technical assistance to country offices to support YF preparedness and response activities</td>
<td>Angola, Namibia, Zambia</td>
<td>UNICEF – EASRO, MoH; WHO</td>
</tr>
</tbody>
</table>
Case Management

Although there is no specific curative therapy for yellow fever, such as antiviral drugs, adequate supportive care is imperative. This strategy and scale up plan will ensure the wide dissemination of simplified case management emergency guidance for yellow fever, as well as retraining of health workers in clinical case management to cover early recognition, management, and referral of severe cases.

Support will be provided for case management, including required logistical support and in the clinical management of suspected, probable and confirmed cases. Laboratory facilities will be strengthened to support clinical management including PCR, IgM and test evaluation services.

Table 11 | Partner Activities- Case Management

<table>
<thead>
<tr>
<th>Key Activity</th>
<th>Location</th>
<th>Partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>Importation of essential medicines and medical supplies to support the pediatric and other hospitals in Luanda and Huambo. GIK supply of basic medicines and supplies in support of the priority needs of the paediatric hospitals over a 12 month period.</td>
<td>Luanda and Huambo, Angola</td>
<td>WVI, MOH, WHO, UNICEF, CDC and MSF (Spain)</td>
</tr>
<tr>
<td>Ensuring access to essential health care for asylum seekers and refugees in coordination with national authorities and partners</td>
<td>Kenya, Rwanda, Tanzania, Uganda, DRC, others</td>
<td>UNHCR</td>
</tr>
<tr>
<td>Preparedness and deployment readiness of Emergency Health Team</td>
<td>DRC - Walikalie, Ituri, North Kivu</td>
<td>Medair</td>
</tr>
<tr>
<td>Comprehensive primary health care support with EPI being supported in 34 clinics in Eastern DRC</td>
<td>DRC - Walikalie, Ituri, North Kivu</td>
<td>Medair</td>
</tr>
<tr>
<td>Selection and mobilization of experts to support outbreak response that fulfil all need in terms of language and field skills</td>
<td>Angola</td>
<td>TEPHINET/REDSUR</td>
</tr>
<tr>
<td>Support resource mobilization and surge capacity for outbreak response</td>
<td>Eastern and Southern African Region</td>
<td>UNICEF - EASRO</td>
</tr>
<tr>
<td>Support to IELE (national Agency in charge of epidemiological surveillance) through the training of district level focal points on case investigation and case management</td>
<td>Gabon</td>
<td>UNICEF - Gabon</td>
</tr>
<tr>
<td>Capacity building of community workers in inter personal communication for yellow fever prevention</td>
<td>DRC</td>
<td>UNICEF – WCARO</td>
</tr>
<tr>
<td>Training of health staff</td>
<td>DRC</td>
<td>Malteser International</td>
</tr>
</tbody>
</table>
STRATEGIC OBJECTIVE 3

Prevent international spread

Coordination and Leadership

The WHO at all three levels (HQ, Regional Office and Country Offices) shall support the objectives through:

- providing technical guidance to countries to conduct rapid assessments, prepare plans, mobilize financial and other resources, and provide advice on implementation
- establishing regional mechanisms for international/cross national actions
- establishing a regional dashboard system with member states to monitor the implementation and progress with these strategies; and
- facilitating partner coordination to ensure synergy of the response actions through strategic planning.

In order to ensure that the epidemic is rapidly controlled, the WHO will specifically:

- strengthen leadership and coordination frameworks using the Incident management system (IMS) at all levels of the organization and in synchrony with national coordination structures at country level
- coordinate, mobilize and deploy staff with appropriate expertise from member states, in collaboration with regional and international partners; The GOARN network, and other partners will be mobilized as necessary
- deploy specialized staff and resources in the affected districts; and
- establish standard operating procedures (SOPs) for response actions

Advocacy is needed for the response at all levels from the global to the local, requiring strong political engagement. Advocacy for adequate domestic financial resources needs to be pursued to contribute for the operational costs. Response teams will be placed in all the provinces and districts for better support to the local authorities. In Kinshasa and at the field level in DRC, WHO will organize coordination meetings and will ensure the coverage of needs and identification of gaps are filled by partners in the health sector.

For the purposes of coordination and leadership to the response, the Incident Management System in Angola, DRC, Uganda and AFRO will be strengthened to fulfil the required functions and expectations. The support to these structures will continue to be drawn from a variety of sources, with tight coordination needed between all three levels of the Incident Management System (led by AFRO) to identify gaps in the recruitment to each IMS, especially in light of the pre-emptive vaccination campaign and required micro-planning.
Table 12 | Partner Activities - Coordination and Leadership

<table>
<thead>
<tr>
<th>Key Activity</th>
<th>Location</th>
<th>Partners</th>
</tr>
</thead>
<tbody>
<tr>
<td>Support to establishing a national EOC/IM system, program planning and implementation</td>
<td>Angola</td>
<td>US- CDC</td>
</tr>
<tr>
<td>Support countries by providing technical assistance in preparation of outbreak preparedness and response plans, campaign preparation &amp; implementation and continuous advocacy with government authorities for strong coordination and resource inputs.</td>
<td>Eastern and Western African region</td>
<td>UNICEF- WCARO, EASRO</td>
</tr>
<tr>
<td>Support monitoring activities at central and province level, engage with mobile population for personal protection and environment hygiene promotion</td>
<td>DR Congo</td>
<td>UNICEF- WCARO</td>
</tr>
<tr>
<td>Coordination and oversight of countries’ preparedness and response</td>
<td>Cape Vert, Congo, DRC, Gabon, Sao Tome</td>
<td>UNICEF- WCARO</td>
</tr>
<tr>
<td>In consultation with the UNICEF ESARO, UNICEF Angola to develop key advocacy messages for use by UNICEF in senior level policy dialogue, and for sharing with the RC and OCHA (the latter, through UNICEF ESARO).</td>
<td>Angola</td>
<td>UNICEF – EASRO, OCHA</td>
</tr>
<tr>
<td>Provide technical assistance to local consultants for supervision, data management at provincial and municipal levels; monitoring and coordination of yellow fever campaigns</td>
<td>Angola, Zambia, Namibia</td>
<td>UNICEF – EASRO</td>
</tr>
<tr>
<td>Liaison with IASC, GOARN, ICG and regional offices’ to monitor, review and update the YF response activities</td>
<td>Global</td>
<td>UNICEF HQ</td>
</tr>
<tr>
<td>Ensuring refugees are included in global coordination framework and preparedness and response strategies</td>
<td>Kenya, Rwanda, Tanzania, Uganda, DRC, others</td>
<td>UNHCR</td>
</tr>
<tr>
<td>Data gathering and coordination with GHC response (logistics cluster coordination)</td>
<td>all at risk, but priority for support to DRC</td>
<td>Medair</td>
</tr>
<tr>
<td>Coordination for current gaps and additional partner needs through in country health advisor to DRC Health Cluster in Kinshasa</td>
<td>DRC</td>
<td>Medair</td>
</tr>
<tr>
<td>Cross border population mobility assessment for 1) identification of high priority mobility affected locations for surveillance and monitoring, and 2) forecasting the potential spread of the disease</td>
<td>Angola and DRC</td>
<td>IOM</td>
</tr>
<tr>
<td>Lobbying with the National Directorate for Public Health to ensure that the official data regularly released is disaggregated by age and sex</td>
<td>Angola</td>
<td>UNFPA Angola</td>
</tr>
</tbody>
</table>
Table 13 | Incident management structure augmentation requirements in AFRO, Angola and DRC

<table>
<thead>
<tr>
<th>IMS</th>
<th>Position</th>
<th>Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>AFRO</td>
<td>Planning and resource forecasting</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Case management</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Logisticians</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Epidemiologists</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>SHOC</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Vector control</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>IVD immunisation expert</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>GIS</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Planning Officer</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Admin-finance officer</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td><strong>TOTAL</strong></td>
<td><strong>11</strong></td>
</tr>
<tr>
<td>Angola</td>
<td>Laboratory support</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Data management</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Planning and resource forecasting</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Epidemiology</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Vaccination</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Social mobilization</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Case management</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Incident Manager</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Team Leads</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Information manager</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Media and press</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Admin - HR support</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Admin - senior</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>IT support</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Admin - general - support</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Driver</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>General logistician</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td><strong>TOTAL</strong></td>
<td><strong>38</strong></td>
</tr>
<tr>
<td>DRC</td>
<td>Data management</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Epidemiology</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Field coordination</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Planning and resource forecasting</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Case management</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Logistician</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Epidemiology</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Vector control</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td><strong>TOTAL</strong></td>
<td><strong>35</strong></td>
</tr>
</tbody>
</table>

WHO will work with neighbouring countries (Congo, Namibia and Zambia) to conduct preparedness assessments and to develop preparedness plans and establish minimum preparedness capabilities in readiness for a yellow fever introduction and/or outbreak. A checklist package will be prepared to support countries with preparedness activities. Through preparedness missions to 10 countries including all neighbouring countries over a three to six month period key preparedness actions shall include the following:

- assessing risks, mapping in-country capacities and development of preparedness plans
- establishing emergency operation centres and strengthening coordination capacity in each country;
- establishing, training and operationalizing Rapid Response Teams (RRTs);
- embedding the community engagement and public awareness components of Yellow fever strategies in country preparedness and response plans
reinforce each country’s national epidemiological surveillance capacity; and
help to build core capacities for the International Health Regulations (IHR) and Integrated Disease Surveillance and Response (IDSR).

**Scale up of human resources**

The WHO and partners will mobilize US $ four million for the planned scale up of HR deployments for Yellow Fever surge capacity to Angola and DRC for a period of 60 days. The cost includes per diem, transport for the experts and catalytic operational costs. This requirement will need to be constantly updated and refined in view of the evolving epidemiological data, and how that affects the proposed plan for pre-emptive vaccination.

**Table 14 | Scale up Plan**

<table>
<thead>
<tr>
<th>Position</th>
<th>Angola</th>
<th>DRC*</th>
<th>Republic of Congo</th>
<th>Total WHO Deployments</th>
<th>Total Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Source of Deployment</td>
<td>Total Requirements</td>
<td>Source of Deployment</td>
<td>Total WHO Deployments</td>
<td>Total Requirements</td>
</tr>
<tr>
<td>Field Coordinator</td>
<td>WHO/AFRO, MOH, GOARN</td>
<td>3</td>
<td>WHO/AFRO/W CO</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Epidemiologist</td>
<td>MOH, GOARN, UNICEF, WHO/AFRO, CDC</td>
<td>11</td>
<td>WHO/AFRO/W CO</td>
<td>1</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Entomologist</td>
<td>Cuban Cooperation</td>
<td>0</td>
<td>WHO/AFRO/W CO</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social Mobilization expert</td>
<td>UNICEF, WHO/AFRO/W CO, WHO/AFRO, CDC</td>
<td>6</td>
<td>WHO/AFRO/W CO</td>
<td>1</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td></td>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Logistiction</td>
<td>WHO/AFRO, WHO/AFRO/W CO</td>
<td>12</td>
<td></td>
<td></td>
<td>18</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk Communication</td>
<td></td>
<td>3</td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Vaccination coordinator</td>
<td>UNICEF</td>
<td>0</td>
<td></td>
<td></td>
<td>6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6</td>
<td></td>
<td></td>
<td>9</td>
</tr>
<tr>
<td>Vaccination experts</td>
<td></td>
<td>0</td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Data Managers</td>
<td></td>
<td>0</td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Vaccination logistician</td>
<td>WHO/HQ, UNICEF</td>
<td>6</td>
<td></td>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Admin support</td>
<td>WHO/AFRO</td>
<td>0</td>
<td></td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>93</td>
<td>38</td>
<td>60</td>
<td>102</td>
</tr>
</tbody>
</table>

*source of deployment not available for DRC*
STRATEGIC OBJECTIVE 4

Prioritize research to improve access to yellow fever vaccine, and to improve the effectiveness of other prevention and control interventions

Operational Review

A joint technical and operational process review of the yellow fever response in Angola and the DR Congo will commence shortly. This rapid review is in accordance with the recommendations of the IHR yellow fever Emergency Committee. It will include an analysis of the current epidemiology, risk assessment, and will generate recommendations for amending the yellow fever outbreak response to prevent further international spread.

In each country, review teams will work with the partners and national counterparts to:

1. Review current status of the disease epidemiology and provide risk assessment for further spread within the country and internationally, including a mapping of priority areas requiring urgent attention;
2. Review the current status of the operational response, to identify gaps and provide recommendations for a scaled up response as well improved operational excellence focusing on early recognition of cases, effective case investigation and risk assessment, case based reporting, vector surveillance and control, planning for and implementation of vaccination campaigns, improved case management, social mobilization and risk communication, cross border interventions to mitigate international spread, and logistic capabilities in support of the response;
3. Review and assess the status of implementation of the YF EC recommendations and recommend solutions;
4. Review the operational organization of the WHO response framework, organizational structure and operations in view of the planned scaled up operations and work with the Country level IMS and WR to recommend feasible solutions to strengthen the WCO IMS in support of the planned scaled up operations;
5. Review the national coordination framework at national and provincial level, including framework for partnerships and provide recommendations to the national government for a scaled up operations to contain the outbreak; and
6. Advocate for and provide evidence based technical and operational guidance for improved and scaled up operations to the MOH, the WHO and partners in respective countries.

It is expected that the output of this review will be a report detailing findings and recommendations for:

1. A scaled up operational response and operational excellence at national and sub-national level with a primary focus on the following areas:
   - Current epidemiology, risks status and priority areas requiring special attention
   - Gaps and needs in the Incident command / management function, including the HR needs for response operations
   - Gaps and needs in operational implementation of technical functions
   - Capacity for planning and forecasting needs
   - Logistics and logistic support
   - Information management and sharing
   - Administration and finance function
   - Existing partnerships and areas for strengthening

REQUIREMENTS (US$)

2.7 M
2. Outline of proposed priority interventions for the immediate (first one month), medium (second month), and for the long term (three months and beyond), agreed upon by national government and all stakeholders.
3. Increased political support for the scaled up operational response to the yellow fever outbreak response measured by endorsement of the proposed recommendations for a scaled up operations.

**Yellow Fever Dose Fractioning**

WHO recognizes that further yellow fever outbreaks will strain available vaccine supplies and cannot be met by increasing the production capacity alone. Therefore, innovative solutions to stretch available supplies are being actively investigated by experts recruited for this response. The dose-sparing option, especially in the context of limited vaccine supply as well as the need to rationalize and quickly immunize a large population in an urban setting to mitigate risks of potential explosion of an outbreak with further risks of exportation elsewhere, is currently the most promising option if implemented strategically and with proper planning and roll out.

The available scientific data from one manufacturer (Bio-Manguinhos) with reduced doses given intramuscularly, and the intradermal administration of a fifth of a dose by another manufacturer (Sanofi Pasteur), provide evidence that the fractional-dose approach is an option to stretch vaccine supplies and ensure that as much of the target population as possible can receive a dose of yellow fever vaccine in case of a further expanding outbreak (i.e., for emergency use).

The data have been reviewed by an ad-hoc expert group formed for the response, and will be reviewed in an upcoming SAGE meeting. In parallel, a research agenda is being prepared to ensure that the remaining questions can be addressed expeditiously, including generalizing the dose-sparing to other manufacturers, generating data on children and infants, and addressing regulatory issues (including a potential label change).

**Further research**

A specific research agenda is being developed for yellow fever diagnosis and vaccine. In addition to this, studies on co-infection of malaria and yellow fever, vaccine adverse effects, and differential diagnosis of negatives cases are being conducted. The development of performance indicators for the Incident Management System is also taking place to assess this aspect of the response.
PART III: ANNEXES

Annex A- List of organizations involved
Annex B- Participating organizations’ funding requirements
## ANNEX A - TABLE OF ORGANIZATIONS INVOLVED

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<th>Organization</th>
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<td>OCHA</td>
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<td>REDR AUSTRALIA</td>
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# ANNEX B: PARTICIPATING ORGANIZATIONS’ FUNDING REQUIREMENTS

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<thead>
<tr>
<th>Organization</th>
<th>Sum of Total Activity Requirement (USD)</th>
<th>Sum of Total HR Requirement (USD)</th>
<th>Sum of Total Requirement (USD)</th>
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**End outbreaks in currently affected countries**

- Through targeted vaccination and other public health measures
- Prevent morbidity and reduce mortality through early case detection and strengthened case management

**Prevent international spread**

1. Through vaccination and other public health measures
2. Through early case detection and strengthened case management
3. For international spread

**Partners and Objectives**

- ECDC
- IFRC
- IMC
- IOM
- Malteser International
- Medair
- REDSUR
- Save the Children
- TEPHINET
- UNHCR
- UNICEF

**Objectives**

- Prevent morbidity and reduce mortality
- End outbreaks
- Prevent international spread
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<th>4. Prioritize research to improve access to yellow fever vaccine, and to improve the effectiveness of other prevention and control interventions</th>
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<td>4. Prioritize research to improve access to yellow fever vaccine, and to improve the effectiveness of other prevention and control interventions</td>
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<td>4. Prioritize research to improve access to yellow fever vaccine, and to improve the effectiveness of other prevention and control interventions</td>
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| US CDC                         | *                                                                                                                        |
| 1. End outbreaks in currently affected countries through targeted vaccination and other public health measures | *                                                                                                                        |
| 2. Prevent morbidity and reduce mortality through early case detection and strengthened case management | *                                                                                                                        |
| 3. Prevent international spread | *                                                                                                                        |
| 4. Prioritize research to improve access to yellow fever vaccine, and to improve the effectiveness of other prevention and control interventions | *                                                                                                                        |

| WVI                            | 500,000                                                                                                                |
| 2. Prevent morbidity and reduce mortality through early case detection and strengthened case management | 500,000                                                                                                                  |

* Partner requirements undisclosed
This report is produced on behalf of the WHO Outbreaks and Health Emergencies Programme and partners.

This document provides the WHO Outbreaks and Health Emergencies’s shared understanding of the crisis, including the most pressing health needs, and reflects its joint health response planning.

The designation employed and the presentation of material in this report do not imply the expression of any opinion whatsoever on the part of the WHO Outbreaks and Health Emergencies Programme and partners concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

www.who.int

http://www.who.int/emergencies/yellow-fever/response/en/

@WHO
Additional documents
1. Introduction

1.1 Background

The current yellow fever outbreaks in Angola and the Democratic Republic of the Congo have highlighted that timely laboratory confirmation of suspected yellow fever cases is an essential part of an effective response.

In 2010, yellow fever case definitions, including criteria for laboratory testing were established by a global expert consultation1. This guidance builds on those yellow fever case definitions, clarifying which tests should be done in outbreak and non-outbreak situations.

Although laboratory testing is an essential part of making a yellow fever diagnosis, final confirmation should be done on a case-by-case basis including analysis of the clinical presentation, epidemiological context, and vaccination history.

1.2 Target audience

This document aims to provide guidance for laboratory staff providing diagnostic testing for yellow fever virus infection. It also provides information about laboratory diagnostics for clinical practitioners managing patients with suspected yellow fever and public health professionals engaged in yellow fever surveillance and control activities.

2. Laboratory diagnostic testing algorithms for countries at risk for yellow fever in Africa

2.1 Countries with outbreaks

During outbreaks, laboratory testing strategies should prioritize confirmation of new instances of local transmission and minimize the number of tests required to avoid overwhelming capacity. Figure 1 provides a means of applying such a strategy.

The basic tests needed for laboratory confirmation of yellow fever during an outbreak are:

- **enzyme-linked immunosorbent assay (ELISA)** to measure yellow fever virus IgM. Other flaviviruses- dengue virus, West Nile virus and Zika virus may give a false positive yellow fever ELISA result so, an ELISA panel for other expected flaviviruses, (as determined by local epidemiology) should be performed as a differential diagnosis.

- **reverse transcription polymerase chain reaction (RT-PCR)** for yellow fever virus. This should be performed on samples collected within ten days of onset of symptoms.

All specimens should be transported to laboratories with appropriate patient information (e.g. age, sex, place of residence, onset of symptoms, vaccination history and travel history). Laboratory test results cannot be interpreted correctly without this information. Blood specimens should be tested as soon as possible, preferably within 24 hours of arrival at the laboratory. The time when blood is collected- that is the length of time after onset of symptoms- affects the interpretation of the results of both tests. Therefore it is important to remember that the time estimate is based on the history given by the patient and may not always be accurate.

Current laboratory tests cannot differentiate between yellow fever virus IgM stimulated by vaccination and that stimulated by infection with yellow fever wild-type virus. Therefore, the laboratory results in people who have received a yellow fever vaccine within 30 days must be interpreted with care (see Figure 2) and assessed on a case by case basis, considering the clinical presentation and epidemiological context along with the laboratory results.

If the national laboratory cannot perform appropriate serology testing for yellow fever virus IgM and/or RT-PCR, specimens should be shipped to a WHO regional reference laboratory (RRL) or the nearest recognized laboratory able to perform these tests (see Annex 1).

In districts where local transmission has not yet been confirmed, blood samples should be taken from all people with suspected cases of yellow fever. If the laboratory has reached maximum capacity, priority should be given to testing specimens from those areas where local transmission has not yet been confirmed. It is not essential to perform serology testing to differentiate between yellow fever and other flaviviruses on specimens from areas where local transmission has already been confirmed. However, all specimens should be properly stored for future analysis if needed.

A suspected case of yellow fever is laboratory-confirmed if the following criteria are met:

- presence of yellow fever virus RNA in blood from a person with no history of recent yellow fever vaccination1

  or

- presence of yellow fever virus specific IgM antibody, absence of other relevant flaviviruses (dengue virus, West Nile virus, Zika virus) and no history of recent yellow fever vaccination.

---

1. RT-PCR for yellow fever is currently validated for blood specimens only. Other specimens including saliva and urine may be validated for RT-PCR testing in the future.
Figure 1. Laboratory testing algorithm for suspected cases during yellow fever outbreaks: unvaccinated people

YF suspected cases

- **RT-PCR**
  - (Blood specimens collected ≤ 10 days of symptom onset)
  - RT-PCR (-)
    - Negative
  - RT-PCR (+)
    - Confirmed case

- **YFV IgM with differential diagnosis**
  - (DENV, WNV, ZIKV)
  - (Blood specimens collected ≥ 3 days of symptom onset)
  - YFV IgM (+) and differential diagnosis (-)
    - Confirmed case
  - YFV IgM (-)
    - Negative
  - YFV IgM (+) and differential diagnosis (+)
    - Send to RRL for PRNT

---

YF = yellow fever; YFV = yellow fever virus; DENV = dengue virus; WNV = West Nile virus; ZIKV = Zika virus; RRL = regional reference laboratory; PRNT = plaque reduction neutralization test

*a* Any person with acute onset of fever, with jaundice appearing within 14 days of onset of first symptoms

*b* If RT-PCR is conducted immediately after onset of symptom (< 3 days), negative cases should be retested 3 days after the onset of symptoms. In people with severe clinical symptom, RT-PCR may be positive for more than 10 days after the onset of symptoms. Urine testing is planned for the future but is not yet validated. When this is introduced it is important to know that when urine is tested by RT-PCR, the period of time after onset of symptoms during which the result may be positive, might exceed 10 days.

*c* Dengue virus, West Nile virus and Zika virus should be considered potential causative agents of symptoms and may test positive for YFV IgM. Depending on the local epidemiological situation, testing for other flaviviruses (ELISA) may need to be performed.

*d* When blood from people with suspected yellow fever is negative on both RT-PCR and YFV IgM testing, they are considered negative for YF. However, a negative result for only one of these tests does not rule out yellow fever infection.

*e* Plaque reduction neutralization test.
Figure 2. Laboratory testing algorithm for suspected cases during yellow fever outbreaks: people who have been vaccinated/people with unclear vaccination history

YF = yellow fever; YFV = yellow fever virus; DENV = dengue virus; WNV = West Nile virus; ZIKV = Zika virus; RRL = regional reference laboratory; PRNT = plaque reduction neutralization test

b If RT-PCR is conducted immediately after onset of symptom (< 3 days), negative cases should be retested 3 days after the onset of symptoms. In people with severe clinical symptom, RT-PCR may be positive for more than 10 days after the onset of symptoms. Urine testing is planned for the future but is not yet validated. When this is introduced it is important to know that when urine is tested by RT-PCR, the period of time after onset of symptoms during which the result may be positive, might exceed 10 days.

c Dengue virus, West Nile virus and Zika virus should be considered potential causative agents of symptoms and may test positive for YFV IgM. Depending on the local epidemiological situation, testing for other flaviviruses (ELISA) may need to be performed.

h This interval may be shortened, especially during outbreaks, as two days may be sufficient for a fourfold increase in YFV IgM titres if specific IgM antibody is released from the immune system²,³,⁴.

i Yellow fever negative: (i) RT-PCR (-) and yellow fever virus IgM (-), or (ii) RT-PCR (-) and no significant increase in YFV IgM/IgG titres with two weeks interval.

ii This algorithm applies only to investigation of suspected cases in districts where local transmission has not yet been detected. In districts that have already confirmed local transmission it is not necessary to differentiate between yellow fever IgM caused by vaccination and that caused by wild YFV, therefore those districts should apply the algorithm in Figure 1.
2.2 At-risk countries with no current outbreak

In at-risk countries that do not have confirmed yellow fever outbreaks, laboratory testing should be used to detect a first (index) case. When blood samples are taken from people who have been recently vaccinated, or whose vaccination status is unknown, testing two samples - an initial acute and a later convalescent sample - can determine whether the presence of IgM is due to yellow fever virus infection. If there is a fourfold increase in the yellow fever virus IgM and/or IgG titres between the acute and convalescent serum specimens yellow fever infection can be confirmed.

In summary, a suspected new case of yellow fever can be laboratory confirmed by one of the following:

- presence of yellow fever virus RNA in blood taken from a person with no history of recent yellow fever vaccination; or
- presence of yellow fever virus-specific IgM antibody and absence of other relevant flaviviruses (dengue virus, West Nile virus, Zika virus) without recent yellow fever vaccination history; or
- a fourfold increase in yellow fever virus IgM and/or IgG titres between acute and convalescent blood specimens; or
- presence of yellow fever neutralizing antibodies and absence of other flaviviruses (dengue virus, West Nile virus, Zika virus) in blood taken from a person with no history of yellow fever vaccination; or
- detection of yellow fever antigen by immunoassay in tissues from a person with no history of recent yellow fever vaccination; or
- isolation of yellow fever virus from blood or tissues from a person with no history of recent yellow fever vaccination.

(See Figure 3 below for more details)

---

**Figure 3. Laboratory testing algorithm for suspected cases in non-outbreak settings**

- **Detection of YF virus antigen or YF virus in tissues**
  - **Confirmed case**

- **RT-PCR (Blood specimens collected ≤10 days of symptom onset)**
  - **RT-PCR (+)**
    - **Confirmed case**
  - **RT-PCR (-)**
    - **Negative**

- **YFV IgM with differential diagnosis (DENV, WNV, ZIKV)**
  - **Blood specimens collected ≥ 3 days of symptom onset**
    - **PRNT with differential diagnosis (DEN, WN, ZIKV)**
      - **Positive**
        - **Confirmed case**
      - **Negative**
        - Paired specimens with 2 week interval (vaccinated case)
          - **Confirmed case (unvaccinated case)**

- **YFV IgM (+) and differential diagnosis (+)**
  - **Confirmed case**

- **PRNT for YFV (+) and differential diagnosis (-)**
  - **Confirmed case**

- **PRNT for YFV (+) and differential diagnosis (+)**
  - **Confirmed case**

- **4 fold increase in YFV IgM/IgG titres**
  - PRNT for YFV (+) and differential diagnosis (+)
    - **Confirmed case**
  - PRNT for YFV (-)
    - **Negative**
  - No significant increase in YFV IgM/IgG titres
    - **Confirmed case**
  - Undetermined flavivirus
    - **Negative**

---

*If RT-PCR is conducted immediately after onset of symptom (< 3 days), negative cases should be retested 3 days after the onset of symptoms. In people with severe clinical symptom, RT-PCR may be positive for more than 10 days after the onset of symptoms. Urine testing is planned for the future but is not yet validated. When this is introduced it is important to know that when urine is tested by RT-PCR, the period of time after onset of symptoms during which the result may be positive, might exceed 10 days.*

* Dengue virus, West Nile virus and Zika virus should be considered potential causative agents of symptoms and may test positive for YFV IgM. Depending on the local epidemiological situation, testing for other flaviviruses (ELISA) may need to be performed.

* This interval may be shortened, especially during outbreaks, as two days may be sufficient for a fourfold increase in YFV IgM titres if specific IgM antibody is released from the immune system.

* Yellow fever negative (i) PCR (−) and yellow fever virus IgM (−), or (ii) PCR (−) and PRNT for yellow fever (−)
If national laboratories cannot confirm yellow fever virus disease, specimens that have tested positive for yellow fever virus IgM should be shipped to a RRL as soon as possible (see Figure 4). When national laboratories introduce RT-PCR for yellow fever on a variety of samples (e.g. blood/serum, saliva and urine) and serology testing able to differentiate between flaviviruses, the algorithm will change.

**Figure 4. Laboratory testing algorithm for suspected cases in non-outbreak settings where capacity to confirm yellow fever virus infection is limited**

![Laboratory testing algorithm](image)

<table>
<thead>
<tr>
<th>Laboratory</th>
<th>Length of time taken (days)</th>
<th>Benchmark</th>
</tr>
</thead>
<tbody>
<tr>
<td>National laboratory</td>
<td>Specimen arrived - specimen tested (yellow fever virus IgM with differential diagnosis, RT-PCR)</td>
<td>≤ 1 day</td>
</tr>
<tr>
<td></td>
<td>Specimen arrived – specimen shipped to RRL</td>
<td>≤ 3 days</td>
</tr>
<tr>
<td>Regional reference laboratories</td>
<td>Specimen shipped from national lab - results received from RRL (yellow fever virus IgM with differential diagnosis, RT-PCR)</td>
<td>≤ 5 days</td>
</tr>
<tr>
<td></td>
<td>Specimen shipped from national lab - results received from RRL (PRNT)</td>
<td>≤ 10 days</td>
</tr>
</tbody>
</table>

3. Shipping specimens

The proper shipment of specimens to a regional reference laboratory with established laboratory networks (e.g. polio, measles, influenza, or the Emerging and Dangerous Pathogens Laboratory Network (EDPLN)) requires advanced planning, appropriate packaging, labelling, documentation and communication between all parties involved. Specimens for molecular or serology testing should be kept at 4-8 °C and if they can be transported within one day to the diagnostic laboratory. If it is expected that transport will take more than one day, serum specimens should be frozen at -20 °C. Improper handling of specimens will affect the quality of the diagnostic results.

See *Manual for the monitoring of yellow fever virus infection* available at: [http://apps.who.int/iris/bitstream/10665/68715/1/WHO_IVB_04.08.pdf](http://apps.who.int/iris/bitstream/10665/68715/1/WHO_IVB_04.08.pdf)

4. Indicators

The following indicators provide benchmarks for determining whether laboratory capacity is sufficient for supporting a yellow fever outbreak response.

5. Guidance development

5.1 Acknowledgements

This guidance was developed by an internal steering group made up of staff from WHO Geneva (Philippe Barboza, Mauricio Bellerferri, Pierre Formenty, Erika Garcia, Margaret Harris, Qui Yi Khut, Miguel Norman Mulders, Dhamari Naidoo, Kyoei Nishino, Susan Norris, William Perea, and Sergio Yactayo); WHO Regional Office for Africa (Yahaya Ali Ahmed, Joseph Nsiari-Muzeyi Biey, Annick Ayélé Dosseh, Richard Ray Luce Jr and Jean-Bosco Ndihokubwayo); WHO Regional Office for the Americas (Jairo Andres Mendez Rico); WHO Regional Office for the Eastern Mediterranean (Humayun Asghar); WHO Regional Office for South-East Asia (Aparna Singh Shah); and WHO Regional Office for the Western Pacific (Franciscus Konings).

The external guideline development group was made up of the following experts who reviewed and revised the initial and the final draft: Maurice Demanou, Centre Pasteur Cameroon, Yaoundé, Cameroon; Barbara Johnson, Centers for Disease Control and Prevention, Atlanta, United States of America; Koichi Morita, Institute of Tropical Medicine, Nagasaki University, Japan; Matthias Niedrig, Robert Koch-Institut, Berlin, Germany; Pedro Fernando da Costa Vasconcelos, Instituto Evandro Chagas, Belem, Brazil; and Herve Zeller, European Centre for Disease Prevention and Control, Stockholm, Sweden.

5.2 Guidance development methods

This guidance builds on the yellow fever case definition developed and published in 2010 (1). This guidance uses the case definition as agreed in 2010 but clarifies which tests should be done in outbreak and non-outbreak situations. An internal steering group (see acknowledgements above) made up of WHO staff in headquarters and regional offices developed the first draft. This was then circulated to an external review group made up of people with expertise in laboratory testing and
virology, from the Americas, Europe, and the Western Pacific region (see acknowledgements for full list), who were identified via WHO collaborating centre networks. The external review group reviewed the draft guidance via email and provided written reviews and comments which were incorporated into the revised document. This document was then reviewed by all participants for a second time and input received incorporated in the final document.

5.3 Declaration of interests

No competing interests were identified from the declarations of interests collected. No specific funds were used to develop this guidance.

5.4 Review date

These recommendations have been produced under emergency procedures and will remain valid until December 2016. The internal steering group who developed this guideline will be responsible for reviewing the contents at that time, and updating it as appropriate.

6. References

### Annex 1. Laboratories for confirmation of yellow fever

<table>
<thead>
<tr>
<th>Region</th>
<th>Laboratory (city, country)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Africa</strong></td>
<td></td>
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<tr>
<td></td>
<td><em>WHO regional reference laboratories for yellow fever</em></td>
</tr>
<tr>
<td></td>
<td>*<em>Institut Pasteur in Dakar (Dakar, Senegal)</em></td>
</tr>
<tr>
<td></td>
<td><em>International Centre for Medical Research in Franceville (Franceville, Gabon)</em></td>
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<tr>
<td></td>
<td><em>Kenya Medical Research Institute (Nairobi, Kenya)</em></td>
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<td></td>
<td><em>National Institute for Communicable Diseases (Johannesburg, South Africa)</em></td>
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<td></td>
<td><em>Noguchi Memorial Institute for Medical Research (Accra, Ghana)</em></td>
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<td></td>
<td><em>Uganda Virus Research Institute (Entebbe, Uganda)</em></td>
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<tr>
<td><strong>Americas</strong></td>
<td></td>
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<tr>
<td></td>
<td><em>Instituto Evandro Chagas (Belem, Brazil)</em></td>
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<tr>
<td></td>
<td><em>Instituto Nacional de Enfermedades Virales Humanas (Pergamino, Argentina)</em></td>
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<tr>
<td></td>
<td><em>Institut Pasteur in French Guiana (Cayenne, French Guiana)</em></td>
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<td></td>
<td><em>Instituto Pedro Kouri (Habana, Cuba)</em></td>
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<tr>
<td></td>
<td><em>Centers for Disease Control and Prevention (Fort Collins, United States of America)</em></td>
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<tr>
<td></td>
<td><em>Centers for Disease Control and Prevention- Puerto Rico (San Juan, Puerto Rico-United States of America)</em></td>
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<tr>
<td></td>
<td><em>Instituto Nacional de Salud (Bogota, Colombia)</em></td>
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<tr>
<td></td>
<td><em>Instituto Nacional de Salud (Lima, Peru)</em></td>
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<tr>
<td><strong>Eastern Mediterranean</strong></td>
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<tr>
<td></td>
<td><em>Central Public Health Laboratory (Cairo, Egypt)</em></td>
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<tr>
<td></td>
<td><em>Central Public Health Laboratory (Khartoum, Sudan)</em></td>
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<tr>
<td></td>
<td><em>Health Laboratory (Tehran, Iran)</em></td>
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<tr>
<td></td>
<td><em>National Institute of Health (Islamabad, Pakistan)</em></td>
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<tr>
<td></td>
<td><em>Public health laboratory (Manama, Bahrain)</em></td>
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<tr>
<td></td>
<td><em>Rafiq Harairi Hospital (Beirut, Lebanon)</em></td>
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<td></td>
<td><em>Virology Lab (Rabat, Morocco)</em></td>
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<tr>
<td><strong>Europe</strong></td>
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<tr>
<td></td>
<td><em>Robert Koch-Institut (Berlin, Germany)</em></td>
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<tr>
<td></td>
<td><em>Bernhard Nocht Institute for Tropical Medicine (Hamburg, Germany)</em></td>
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<tr>
<td></td>
<td><em>The State Research Center of Virology and Biotechnology VECTOR (Novosibirsk, Russia)</em></td>
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<tr>
<td></td>
<td><em>Institut Pasteur in Paris (Paris, France)</em></td>
</tr>
<tr>
<td></td>
<td>*Rare and Imported Pathogens Laboratory, Public Health England (London, the United Kingdom)</td>
</tr>
<tr>
<td></td>
<td><em>Russian Research Anti-Plague Institute «Microbe» (Saratov, Russia)</em></td>
</tr>
<tr>
<td><strong>South East Asia</strong></td>
<td><em>National Institute of Virology (Pune, India)</em></td>
</tr>
</tbody>
</table>

*WHO regional reference laboratories for yellow fever*
Q&A: Fractional doses of the yellow fever vaccine
19 June 2016

What is the fractional dose of the yellow fever vaccine?

There is currently a shortage of the yellow fever vaccine. Experts advise that a smaller dose of the vaccine can protect people from the disease. Studies show that the yellow fever vaccine, given as one fifth of the regular dose still provides full immunity against the disease for at least 12 months and likely longer.

This emergency, short-term measure, known as fractional dosing or dose sparing, could be used to control an outbreak in cases where the vaccine supply is limited.

- More Q&A's on yellow fever

What are vaccine experts saying about fractional dosing?

After reviewing evidence, WHO’s Strategic Advisory Group of Experts (SAGE) on Immunization, determined that a fifth of a standard vaccine dose can provide full protection against the disease for at least 12 months and can be used to control outbreaks.

Fractional dosing is not proposed for routine immunization, as there is not enough data available to show that lower doses confer life-long protection. More studies are needed to determine how long this immunity would last beyond 12 months.

- Lower doses of yellow fever vaccine could be used in emergencies

Why is WHO proposing the use of fractional dosing as an emergency measure?

Yellow fever is a serious disease for which there is no specific treatment. The yellow fever vaccine is the best way to protect people at risk. Because of the unprecedented nature and scale of the current outbreak in Africa, existing stockpiles cannot keep up with the increased demand.

In the first 6 months of 2016 alone, WHO and partners sent more than 19 million doses of the vaccine to Angola, Democratic Republic of the Congo, and Uganda for outbreak response. This is 3 times the volume kept in the yellow fever emergency stockpile usually maintained at 6 million doses for an outbreak.

The 4 manufacturers who supply the yellow fever vaccine are working to replenish the global emergency stockpile, but the production process takes a minimum of 6 months.

As more people need the vaccine urgently, WHO, experts and affected governments will use the fractional dose for mass vaccination campaigns to protect more people. The Democratic Republic of the Congo with WHO and partner support are planning a vaccination campaign using fractional dosing in the city of Kinshasa, which has an estimated population of 10 million people and has reported cases of yellow fever. There are concerns that there is the potential for a large-scale outbreak in Kinshasa that could spread to other urban settings. Mass vaccination is the best method of preventing an outbreak in this setting.

Using fractional dosing is the best way to stretch vaccine supplies and protect as many as 8 to 10 million people as soon as possible to stop the spread of yellow fever before the long rainy season begins in October.

- Yellow fever global vaccine stockpile in emergencies
**Will people who receive the emergency dose get a yellow fever certificate?**

This fractional dose will not entitle people to a yellow fever certificate valid for international travel. Until more data is gathered about the duration of protection provided by the fractional dose, people who want to travel internationally, require a full dose of the vaccine. The full dose provides life-long immunity and entitles them to an international yellow fever certificate.

**Can children receive a fractional dose of the yellow fever vaccine?**

There is currently no available data to show that a fractional dose of the yellow fever vaccine in children under 2 years of age will provide the same protection as the full dose. Very young children may have a weaker immune response to the vaccine than older people. Therefore, children under 2 years of age should be offered a full dose.

**How will vaccination records be kept?**

WHO recommends that countries keep good vaccination records of people receiving the fractional dose so that they can be followed up later to assess how long the vaccine protection lasts and be revaccinated if necessary. These people will need to be informed that they have received the fractional dose and will require a full dose of the vaccine if they wish to travel.

**Will people receive the full dose later?**

As soon as the current outbreak is brought under control, the full dose of the vaccine should be used in routine vaccination programmes. People who received a fractional dose may need a booster vaccination later.

**Is there a greater risk of adverse effects with a lower dose of the vaccine?**

The fractional dose comes from the same full dose vaccine. It has been given to millions of people to prevent yellow fever in the past. It is as safe and as effective as the full dose of the vaccine.

Severe adverse effects following a full dose of yellow fever vaccine are extremely rare (less than one per one million people). There is no evidence of increased severe adverse effects when using a fractional dose.

**Has this method been used for other vaccines?**

Fractional dosing is currently being used for inactivated polio vaccine (IPV), Rabies and Bacillus Calmette–Guérin (BCG), a vaccine primarily used against tuberculosis.
Fractional dose yellow fever vaccine as a dose-sparing option for outbreak response

WHO Secretariat information paper

20 JULY 2016

This document was produced by
the Department of Immunization, Vaccines and Biologicals
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1. Preamble
This document represents the World Health Organization (WHO) Secretariat position on the use of yellow fever (YF) vaccine in the context of supply shortages in response to the current outbreak in Africa in 2016. The development of this paper was led by the WHO Initiative for Vaccine Research with contributions to specific sections from the WHO Departments of Pandemic and Epidemic Diseases, Essential Medicines, and Immunization Vaccines and Biologicals. The evidence and the proposed recommendations, reflected in this document, has been discussed with YF experts and reviewed by the WHO Strategic Advisory Group of Experts (SAGE) on Immunization. SAGE and the YF experts provided input to this paper. The recommendations were vetted by SAGE, but they don’t represent a formal SAGE recommendation. The paper will be updated as additional data become available. A full review on the use of fractional dose YF vaccine will be conducted by SAGE in October 2016.

2. Introduction
Ongoing YF outbreaks are sharply increasing the demand for YF vaccine, exhausting the global stockpile and putting at risk the immunization of endemic populations. The campaigns currently planned have led to a shortage of the vaccine, a situation which could deteriorate further should expansion of outbreaks necessitate additional immunization campaigns on a large scale. An assessment of existing opportunities to increase the availability of vaccine in response to ongoing outbreaks is therefore urgently required. This paper reviews the evidence on dose-sparing strategies through fractional dosing of YF vaccine as an immediate and short-term option to meet the needs of large-scale campaigns, and proposes recommendations for fractional dose vaccination in case of imminent need in the context of outbreak response. The paper is intended to support efforts to introduce YF vaccine fractional dose use in situations where supply capacity is threatened or inadequate, e.g. following the spread of YF into densely populated areas. This is not proposed as a longer-term strategy or to replace established routine immunization practices.

3. Background
YF is a mosquito-borne viral disease of humans, which can be asymptomatic or cause a wide spectrum of disease, from mild symptoms to severe illness with bleeding, jaundice and, ultimately, death. Wild-type YF virus induces lifelong protection against subsequent infection. YF is endemic in countries in the tropical regions of Africa and South America. The vast majority of reported cases and deaths (>90%) occur in sub-Saharan Africa, where YF is a major public health problem occurring in epidemic patterns. Based on data from 32 Yellow Fever endemic African countries, analysis suggests an annual burden of 84 000 – 170 000 severe cases and 29 000 – 60 000 deaths due to YF in the year 2013.

Due to the existence of an enzootic sylvatic transmission cycle among non-human primates, the disease cannot be eradicated. However, prevention through vaccination can limit the morbidity and mortality of the disease. There are

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two immunization strategies: (1) delivery of YF vaccine in endemic settings via routine childhood immunization programmes, and (2) mass vaccination campaigns to catch-up on immunization in unvaccinated cohorts not eligible for routine immunization, or in response to an outbreak of the disease.

YF vaccination is very effective, but where implementation of recommended immunization has been suboptimal or even non-existent in some countries, the disease has recurred, leading to major outbreaks in countries where YF was considered to be under control or had disappeared.

By definition, YF outbreaks may constitute one or more cases. Currently, YF outbreaks are ongoing in Africa (Angola, Democratic Republic of the Congo (DRC) and Uganda) as well as in South America (Brazil, Colombia, and Peru). As of 7 June 2016, 2945 suspected cases and 329 deaths were reported from Angola, of which 819 cases and 108 deaths were laboratory confirmed. In DRC, 57 cases were confirmed as of 7 June, of which 51 were imported from Angola, 6 were autochthonous (2 Kinshasa, 1 Kwango, 1 Congo Central; and 2 from the Northern provinces which were not related to this outbreak). In Uganda, as of 7 June, a 61 suspected cases and 7 confirmed cases were reported. The most recent situation report is available on the WHO website.iii Imported cases among unvaccinated individuals have been reported from China (11 cases), Morocco (1 suspected case) and Kenya (2 cases).

4. International Health Regulations (IHR 2005)

YF is the only disease specified in the International Health Regulations (IHR) for which countries may require proof of vaccination from travellers as a condition of entry under certain circumstances and may take certain measures if an arriving traveller is not in possession of a YF vaccination certificate. WHO publishes an annually updated list of countries with risk of YF transmission and countries requiring YF vaccinationiv. However, in practice, the vaccination requirements are unevenly applied; for example many international workers in Angola were not vaccinated at the start of the current outbreaks. To interrupt the international spread, it is urgent and essential that the provisions in the IHR be rigorously enforced by requiring travellers to present YF vaccination certificates when entering the countries where this is mandatory. The feasibility of implementing this measure at land crossings remains a challenge, and may not be logistically feasible given the porous borders at land crossings.

Annexes 6 and 7 to the IHR stipulate that the YF vaccine used must be approved by WHO. Annex 7 was amended in 2014v to indicate that a single dose of the vaccine is enough to confer immunity for life, removing the need for booster vaccination after 10 years, and that the vaccination certificate remains valid throughout the life of the person vaccinated. This amendment entered into force on 11 July 2016, and all countries are required to abide by the new requirementvi.

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v World Health Assembly Resolution WHA 67.13
vi http://www.who.int/ith/annex7-ihr.pdf?ua=1, accessed June 2016
Under the auspices of the IHR, an Emergency Committee concerning YF was convened by the WHO Director-General on 19 May 2016. The Director-General accepted the Committee’s assessment that the current YF situation is serious and of great concern and requires intensified control measures, and urged Member States to enforce the YF vaccination requirement for travellers to and from Angola and the DRC in accordance with the IHR, as set out in Annex 7vii.

Recognizing that the supply of YF vaccines is limited, the Committee advised the immediate application of the policy of 1 lifetime dose of YF vaccinev and the rapid evaluation of YF vaccine dose-sparing strategies by the WHO SAGE. This information paper is prepared to brief SAGE in case of an emergency in which SAGE will be asked to provide their advice on dose-sparing options. A formal evaluation by SAGE is envisaged for October 2016.

Fractional-dose administration of YF vaccine, as discussed in this paper, should not be considered equivalent to full-dose vaccination, and until further data have been generated it does not constitute a sufficient dose for YF vaccination as required by the IHR.

5. Vector control measures

The incidence of YF is increasing, especially due to infection in metropolitan areas with growing human population densities and urban environments that provide mosquitoes with various oviposition sites. Increased urbanization, particularly among poorer sections of the population without access to a proper water supply and basic health services, and an increase in international travel, both have the potential to contribute to increased densities of Aedes aegypti, the vector of YF virus.

There are no specific data available on vector control measures used in the context of implementing YF vaccination. However, well implemented vector control programmes using existing tools and strategies have been found to be effective in reducing the transmission of Aedes-borne diseasesviii, and can therefore contribute to risk reduction. Improving the quality and extent of implementation of vector control interventions can ensure improved impact against Aedes-borne diseases such as YF. In low resource settings, country commitment, intersectoral collaboration and capacity building for entomological surveillance, as well as sustained effective YF control and a rapid outbreak response, are critical factors for strengthening vector control.

Interventions to reduce the risk of YF virus transmission include: targeted residual spraying on Aedes mosquito resting sites; space spraying inside houses where Aedes mosquitoes rest and bite; larval control through source reduction and use of larvicide; and personal protection measures using appropriate repellent and clothing. Vigorous promotion and implementation of vector control measures and appropriate personal protective measures can reduce the risk of exposure to circulating YF virus.

6. Yellow fever vaccine characteristics

YF vaccines are recommended to be given as a single dose (0.5 ml) administered by subcutaneous (SC) or intramuscular (IM) inoculation. The evidence in this briefing note is mostly derived from data on vaccination by the SC route. Healthy individuals almost always develop neutralizing antibodies after vaccination. Clinical trials have found that 80%–100% of vaccine recipients develop protective levels of neutralizing antibodies within 10 days and 99% do so within 30 days. Protection appears to be life-long. Limited data suggest that seroconversion is somewhat lower in children <2 years of age, but the clinical relevance of this is uncertain.\textsuperscript{ix} No evidence on potential differences in immunogenicity and efficacy between SC and IM administration could be identified.

All the current commercially available YF vaccines are live attenuated viral vaccines from the 17D lineage. According to current WHO recommendations on quality, safety and efficacy of live attenuated YF vaccines\textsuperscript{x} the immunizing dose recommended for use should not be less than 3.0 log\textsubscript{10}, i.e. 1000 international units (IU). The release specifications should be approved by the National Regulatory Authorities (NRA).

There are two YF sub-strains in use currently for manufacture of YF vaccine, namely YF 17DD and YF 17D-204. YF 17D-213 is a derivative of 204, but differs significantly as it has gained a glycosylation site in the E protein. Of these sub-strains, 17D-204 is used by Sanofi and by Institut Pasteur, Dakar, (at different passage levels), 17D-213 is used by Federal State Unitary Entreprise of Chumakov Institute, and 17DD is used by Bio-Manguinhos, Brazil.\textsuperscript{x} Therefore, any extrapolation of clinical trial data between different products, in particular of different sub-strains, should be done with caution.

7. Fractional-dose yellow fever vaccine immunogenicity when administered by subcutaneous, intramuscular or intradermal injection

Two recent reviews on dose-sparing strategies were considered. (1) A review of the evidence for a dose-sparing strategy for YF vaccine by ID administration was conducted by the Program for Appropriate Technology in Health (PATH) in 2013. The authors concluded that this approach could be implemented in the short to medium term, provided that clinical evidence for non-inferiority, safety, and dose levels has been generated. It could also be useful in public health emergencies if an acute shortage of YF vaccine occurs. (2) A systematic review by WHO of recent evidence on fractional dose administration of YF vaccine via the usual routes (SC or IM) and by ID injection. Since the review by PATH additional scientific data were generated by Martins et al (2013) and Campi-Azevedo et al (2014). The WHO search strategy is outlined in Annex 1.

\textsuperscript{ix} Gotuzzo E. et al., Efficacy and duration of immunity after yellow fever vaccination: systematic review on the need for a booster every 10 years. Am J Trop Med Hyg 2013

\textsuperscript{x} WHO TRS 978 Annex 5 \url{http://www.who.int/biologicals/expert_committee/TRS_978_61st_report.pdf}, accessed May 2016
While the study by Lopes et al dates from 1988, there are two recent vaccine trials which examined safety and immunological non-inferiority: Roukens et al (2008) studying the ID administration of YF vaccine, and Martins et al (2013) and Campi-Azevedo et al (2014) studying IM/SC vaccine administration (same cohort, but different analysis). All studies demonstrated seroconversion and geometric mean titres (GMT). Fractional dose via IM/SC and by ID delivery showed similar immunogenicity as the full dose. Table 1 summarizes the findings in these studies.
### Table 1: Studies assessing immunogenicity of fractional dose YF vaccine administered by SC/IM or ID inoculation.*

<table>
<thead>
<tr>
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<tbody>
<tr>
<td><strong>Study site</strong></td>
<td>Rio de Janeiro, Brazil</td>
<td>The Netherlands</td>
<td>Rio de Janeiro, Brazil</td>
<td>Rio de Janeiro, Brazil</td>
</tr>
<tr>
<td><strong>Dose-sparing approach and route of delivery</strong></td>
<td>Fractional dose, IM/SC</td>
<td>Fractional dose, ID vaccination</td>
<td>Fractional dose, IM/SC</td>
<td>Fractional dose, IM/SC</td>
</tr>
<tr>
<td><strong>YF vaccine</strong></td>
<td>All YF vaccines came from the same seed lot and complied with WHO minimum requirements for biological substances (1976)</td>
<td>All administered vaccines originated from Stamaril, Lot # Y5597, Sanofi Pasteur, France.</td>
<td>Experimental products by Bio-Manguinhos having 6 different viral particle concentrations in IU/dose.</td>
<td>Bio-Manguinhos, same vaccine recipients and study #3</td>
</tr>
<tr>
<td><strong>Fractional dose</strong></td>
<td>1/5&lt;sup&gt;th&lt;/sup&gt; of 1000 PFU</td>
<td>1/5&lt;sup&gt;th&lt;/sup&gt; of full dose (which was 3.5 x 10&lt;sup&gt;3&lt;/sup&gt;PFU)</td>
<td>Full dose of 27,476 IU (NIIBSC reference) and five lower alternative formulations (31IU, 158IU, 587IU, 3013IU, 10447IU)</td>
<td>Full dose of 27,476 IU (NIIBSC reference) and five lower alternative formulations (31IU, 158IU, 587IU, 3013IU, 10447IU)</td>
</tr>
<tr>
<td><strong>Sample Size</strong></td>
<td>259 healthy males</td>
<td>175 participants, healthy adults of 18 years and older (up to 70, mean age 25-27)</td>
<td>749 healthy, adult, army males, not previously vaccinated against YF, mean age 19.4y; around 90% of subjects were seropositive for Dengue virus and 12-23% for YF at baseline (the latter excluded from PP analysis)</td>
<td>749 healthy, adult, army males, not previously vaccinated against YF; mean age 19.4 years</td>
</tr>
<tr>
<td><strong>Study design</strong></td>
<td>Volunteers were allocated to each vaccine group in the order in which they reported for inoculation</td>
<td>Randomized controlled trial to test for immunological non-inferiority. Participants received ID vaccination 0.1ml or SC vaccination 0.5ml. 155 were primary vaccinated participants (primovaccinees), 20 revaccinees</td>
<td>A double blind, randomized clinical trial to test for immunological non-inferiority.</td>
<td>Randomized control trial. Compared kinetics of biomarkers (serum chemokine and cytokine) triggered by the full dose and the five lower alternative subdoses of currently used full doses of 17DD YF vaccine.</td>
</tr>
<tr>
<td><strong>Follow up period</strong></td>
<td>28 days</td>
<td>10 months</td>
<td>1 year</td>
<td>1 year</td>
</tr>
<tr>
<td><strong>Data collection</strong></td>
<td>The amount of PFU and LD&lt;sub&gt;50&lt;/sub&gt; required to induce seroconversion were assessed by 8 different varying doses of vaccine. Blood samples were obtained before and 28 days after vaccination. No peak time.</td>
<td>Virus neutralization 80% and virus RNA were evaluated to assess the vaccine efficacy. Primovaccinees: Blood samples were collected before vaccination, 4 wks and 8 wks after vaccination. Revaccinees: Blood samples were collected before vaccination, 5 d and 2 wks and 1 yr after vaccination.</td>
<td>PRNT 50%, viral RNA, and GMTs were evaluated to assess the vaccine efficacy. The occurrence of adverse events was evaluated among volunteers who recorded them on their diaries during the first 10 d after vaccination. No peak time.</td>
<td>PRNT, virus RNA, chemokines and cytokines were evaluated to assess the vaccine efficacy as follows: PRNT80%: Day 0, 30, 365; RT-PCR: Day 3, 4, 5, 6, 7 Chemokines &amp; Cytokines: Day 0, 3, 4, 5, 6, 7, 15, 30</td>
</tr>
<tr>
<td><strong>Vaccine Efficacy (defined as seroconversion and immune response titres)</strong></td>
<td>The inoculation of 200-500 PFU induced seroconversion in 100% of participants. The amount is much lower than the minimum required standard by WHO of 1000 PFU. From 2 wks to 1 yr after vaccination, the maximum serum dilution (1:16) at which 80% of virus plaques were neutralized did not differ between those given a reduced ID or standard SC dose. In all cases the WHO standard of seroprotection was reached.</td>
<td>Seroconversion: 97% (except fractions lower than 587 IU). The duration of immunity had no statistically significant difference among groups except 31 IU group.</td>
<td>A less than 1/46&lt;sup&gt;th&lt;/sup&gt;-fold dose of YF vaccine (587 IU) is able to trigger similar immunogenicity, as evidenced by significant titres of anti-YF PRNT. Analysis of serum biomarkers in association to PRNT and viraemia, support 10-fold lower subdose (3013 IU) of 17DD YF vaccine.</td>
<td></td>
</tr>
<tr>
<td><strong>Vaccine Safety</strong></td>
<td>No description</td>
<td>Redness, swelling and itching were reported more by ID group. 3 SC participants rated events as severe.</td>
<td>No serious adverse events were reported from any groups.</td>
<td>No description</td>
</tr>
<tr>
<td><strong>Other findings</strong></td>
<td>No difference in immunogenicity observed between females and males, Doses below 587 IU (158 and 31IU) were inferior to full dose; viraemia unrelated to vaccine dose</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Limitations</strong></td>
<td>Small sample size, no stratification by age, modified PRNT.</td>
<td>Small non-representative population, and narrow age range</td>
<td>Small non-representative population, and narrow age range</td>
<td></td>
</tr>
</tbody>
</table>

*For risk of bias assessments, see Annex 3. Unit of potency presented as in the publication.*
Intradermal administration of a fractional dose

Roukens et al demonstrated that ID injection of 17D-204 YF vaccine with 1/5\(^{th}\) of 0.5ml (full dose) was equally immunogenic compared to the SC delivery of a full dose (6). In this randomized control trial participants received 0.1 ml (1/5\(^{th}\) of full dose) ID or 0.5ml SC. From 2 weeks to 1 year after vaccination, the maximal serum-dilution at which 80% of virus plaques were neutralized (i.e. neutralizing antibody titres) did not differ between vaccinees given a reduced ID or standard SC dose. In all cases the WHO standard of seroprotection was reached (see GRADE table 2, Annex 2).

Fractional dose using the normal route of SC administration

Lopes O et al showed that seroconversion occurred following administration of 17DD YF vaccine in 100% of the participants in 28 days with 1/5\(^{th}\) to 1/2 of the WHO standard dose; but the vaccine was based on older vaccine formulations of the product and therefore of limited interest. The recent randomized controlled trial assessing fractional dosing via regular route of administration using 17DD YF vaccine produced by Bio-Manguinhos (Martins et al, 2013; Campi-Azevedo et al, 2014) are of greater interest. Martins et al showed that even a 46x dilution resulted in equivalent humoral response as that induced by the full dose. Seroconversion occurred in 97% of the participants at 30 days with 1/46\(^{th}\) of the full dose, and neutralizing antibody titres reached equivalent levels to those induced by the full dose.

Campi-Azevedo et al carried out further investigation into viraemia and chemokine and cytokine responses. The viraemia pattern was equivalent to that with the full dose down to a dilution of 1/9 (3013 IU), whereas with the 1/46 dilution (587 IU) there was a somewhat reduced and delayed viraemia peak. For the 1/46 dilution, slight differences were also seen in relation to pro-inflammatory cytokines, while serum cytokines were equivalent to those following the full dose (8).

It should be noted that the Martins/Campi-Azevedo studies used vaccine of high potency of above 10 000 IU (27 476 IU), and hence even the nine-fold dilution contained three times more IU than the lower threshold recommended by WHO. In addition, the exact method of determination of potency is not described. This is important since a considerable range of potency in routine vaccine batches has been reported from all manufacturers (WHO informal consultation on the minimum potency specifications for YF vaccines, 2007) ranging from 1995 \(\log_{10}\) IU to 2 511 886 \(\log_{10}\) IU/dose (a more than 1000-fold difference). Hence interpretation of non-inferiority results seen with fractional doses need to be normalized by the actual vaccine potency expressed in IU.

In summary, the above findings are encouraging and document the potential of fractional dosing (see GRADE table 1, Annex 2). Based on the data from Martins and Campi-Azevedo, a fraction dose containing about 3000 IU could be considered equivalent to a full dose and should be considered as preferential dose potency for fractional vaccine doses. Below this value (about 3000–600 IU), protection, but possibly less than life-long protection, needs to be assumed. Dose fractioning below a potency of about 1000 IU/dose is not advisable, in order to leave a safety margin to 600 IU below which the humoral immune response was inferior to that with higher potency doses.
The limitations to the evidence available are the following:

- Study populations are likely different from the populations living in YF endemic areas, both in relation to flavivirus exposure and genetic background.
- SC immunization data are only available from one manufacturer using YF 17DD vaccine.
- Children and immunocompromised populations (and women for the fractional dosing (IM/SC) are not included in the studies to evaluate immunogenicity and safety in these subpopulations.
- Long-term duration of immunity beyond one year is unknown with a dose-sparing approach.

Actual doses of YF virus particles in each lot of all prequalified vaccines are different and vary across lots and stage of expiry, which is important to address if considering the use of a fractional dose.

8. Yellow fever vaccine safety when administered as a fractional dose

The most common systemic side effects after full dose YF vaccination include headache, asthenia, myalgia, malaise, fever, rash and chills. Urticaria is uncommon. Allergic reactions are extremely rare, occurring at an incidence of less than 1 per million, principally in persons with known egg sensitivity\textsuperscript{xii}. In clinical trials, non-serious adverse events were reported by 25% of vaccinees receiving a full dose of YF vaccine. Serious adverse events following immunization (AEFI) with a full dose of YF vaccine are rare (1 per 2 million people vaccinated in preventive campaigns).

Serious adverse events related to vaccination include YF vaccine-associated viscerotropic disease, neurological diseases, and severe hypersensitivity reactions. The available data suggest that the incidence of acute viscerotropic disease following YF vaccination ranges from 0 to 0.21 cases per 100 000 vaccine doses in regions where YF is endemic, and from 0.09 to 0.4 cases per 100 000 doses in populations not exposed to the virus. Neurological (or neurotropic) disease is estimated to occur with a frequency of 0.8 cases per 100 000 vaccine doses administered.\textsuperscript{xii, xiii}

The available data on adverse reactions after fractional doses of YF vaccine are limited to the studies described above and the number of persons vaccinated is too low to appropriately assess the rate of rare but serious adverse events (SAE). A recent study\textsuperscript{xiv} to compare the immunogenicity and safety of 5 alternative formulations of YF vaccine with lower concentrations of virus particles reported no SAE attributable to the vaccine. It is, however, difficult to draw conclusions on SAE with this small sample size. Headache and fatigue were the most frequent symptoms, being reported by more than 1/5\textsuperscript{th} of volunteers. Among 749 volunteers in the study, over 15% reported fever ≥ 37.5 °C and 2% ≥ 39 °C. Pain,

\textsuperscript{x} Vaccines, SIXTH EDITION, STANLEY A. PLOTKIN
\textsuperscript{xii} Detection and investigation of serious adverse events following yellow fever vaccination. Guidance from an informal consultation of experts. 18–19 November 2008. Geneva, Switzerland
\textsuperscript{xiii} Risk of yellow fever vaccine-associated viscerotropic disease among the elderly: a systematic review. Rafferty et al Vaccine 2013, 31(49):5789-805
\textsuperscript{xiv} 17DD yellow fever vaccine A double blind, randomized clinical trial of immunogenicity and safety on a dose-response study Reinaldo M. Martins et al
arthralgia, pruritus and nausea were also reported. There were no differences in the frequency of common adverse events, with exception of pain, experienced more frequently with the full dose vaccine.

In another study, in 155 primovaccinated participants, ID vaccination evoked redness and swelling at the site of inoculation more frequently and for a significantly longer period than after subcutaneous vaccination. Itching at the site of injection was also reported more by ID vaccinees. The subcutaneously primovaccinated participants reported significantly longer pain at the site of injection and also myalgia compared to the fractional dose. The severity of adverse events due to vaccination, which was reported on a 4-level scale (−, +/-, +, ++), did not reveal a difference in experienced discomfort (both local and systemic) between the ID and SC group.

It has been argued that lower doses of live flavivirus vaccines might be associated with deleterious safety effects. This is primarily based on the observation that vaccine virus viraemia does not correlate with infectious dose. A common explanation is that high virus replication compensates for a small inoculum. However, Campi-Azevedo et al showed that intensity of viraemia stays the same with all fractional dose steps down to 3000 IU, and does not increase and is of the same duration at lower doses. Furthermore, a direct correlation of lower doses of YF vaccine with increased reactogenicity or SAEs has not been described and there are no data to indicate an increase of severe side effects (viscerotopic complications) when using a fractional dose. However, active surveillance to report and respond to AEFIs is recommended during the introduction of YF vaccines in fractional doses.

9. Considerations related to regulatory approval

Exploring alternative potential strategies on dose optimization of YF vaccine to increase supply or surge capacity is of critical importance for deployment of the vaccine in outbreak control. The recommendations on fractional dose administration of YF vaccine discussed in this paper constitute an off-label use of the vaccine. Vaccine administration via the ID route is also an off-label use of the vaccine. Risk management of the proposed use of a fractional dose should be addressed as well as all implications on a short and long term basis that require clinical, regulatory and programmatic assessments. Regulatory strategies are lengthy and may be promising in the medium or long term but cannot be considered as solutions in the short term for off-license and emergency use.

Considering that available data are restricted to specific manufacturers and their specific viruses, and that variability of the manufacturing process results in different vaccine titres, extrapolation to all YF vaccines requires careful consideration. Product-specific data are needed to support regulatory

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\textsuperscript{xv} Intradermally Administered Yellow Fever Vaccine at Reduced Dose Induces a Protective Immune Response: A Randomized Controlled Non-Inferiority Trial. Anna H. Roukens et al Plos One. 2008; 3(4): e1993

\textsuperscript{xvi} Innate and adaptive cellular immunity in flavivirus-naive human recipients of a live-attenuated dengue serotype 3 vaccine produced in Vero cells (VDV3). Sanchez V. et al, Vaccine 2006

approval and subsequent prequalification of the new dose. Dose reduction initiatives must be accompanied by relevant stability data and clinical data.

As a medium-term strategy to increase vaccine supply, exploration of the introduction of an upper potency limit should be considered by manufacturers and regulators. This approach is already practiced by one manufacturer. If a manufacturer needs to change the target potency during manufacturing, then it would be necessary to demonstrate to the NRA and later prequalified, that there is no impact of this change on the quality and efficacy of the vaccine, as well as no impact on its shelf-life.

Regarding the rubber seal (septum) of multidose vials and its resistance to multiple punctures, no specific prequalification guidelines are available. At national level, ISO or pharmacopeia standards are being applied. No direct evidence could be retrieved on the durability of the rubber seal when applying more punctures than indicated per multidose vial. Appropriate monitoring of any programmatic issues in practice should be included in campaigns as a precautionary measure. Currently, trials on fractional dose use with IPV are ongoing in India; these may provide lessons on practical aspects of fractional dose use with 10-dose vials.

10. Programmatic considerations

Members of the WHO Immunization Practices Advisory Committee (IPAC) provided insight on the following programmatic considerations via an informal consultation.

The four WHO prequalified YF vaccines are currently available in multidose vials containing 2, 5, 10, and 20 doses that need to be reconstituted with excipient diluent (water or saline, depending on manufacturer). Before reconstitution, the lyophilized vaccine can be stored at 2–8 °C for a period of up to 2 or 3 years (see Table 2). The vaccine vials carry a vaccine vial monitor type 14 (VVM 14), which indicates that the lyophilized vaccine can withstand cumulative exposure to 37 °C for up to 14 days without loss of potency. Due to the limited heat stability of YF vaccine after reconstitution, opened multidose vials of YF vaccine must be kept at 2–8 °C, and must be discarded at the end of the immunization session, or within six hours of opening, whichever comes first.
Table 2: WHO prequalified YF vaccines and their characteristics

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Vial Size (doses)</th>
<th>VVM type</th>
<th>Shelf Life (months)</th>
<th>Indicated storage Temperature</th>
<th>Cold chain volume (cm$^3$ per dose)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sanofi Pasteur</td>
<td>10</td>
<td>14</td>
<td>36</td>
<td>2–8 °C</td>
<td>2.46</td>
</tr>
<tr>
<td>Bio-Manguinhos</td>
<td>5</td>
<td>14</td>
<td>24</td>
<td>2–8 °C</td>
<td>6.31</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>14</td>
<td>36</td>
<td>2–8 °C</td>
<td>2.96</td>
</tr>
<tr>
<td></td>
<td>50 (currently not available)</td>
<td>14</td>
<td>24</td>
<td>2–8 °C</td>
<td>0.63</td>
</tr>
<tr>
<td>Chumakov Institute</td>
<td>2 (very limited, for travellers)</td>
<td>14</td>
<td>24</td>
<td>2–8 °C</td>
<td>7.2</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>14</td>
<td>24</td>
<td>2–8 °C</td>
<td>6.0</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>14</td>
<td>24</td>
<td>2–8 °C</td>
<td>3.6</td>
</tr>
<tr>
<td>Institut Pasteur Dakar</td>
<td>5</td>
<td>14</td>
<td>36</td>
<td>2–8 °C</td>
<td>2.8</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>14</td>
<td>36</td>
<td>2–8 °C</td>
<td>1.4</td>
</tr>
<tr>
<td></td>
<td>20 (upon request)</td>
<td>14</td>
<td>36</td>
<td>2–8 °C</td>
<td>0.7</td>
</tr>
</tbody>
</table>

Administered as a full dose, YF vaccines are injected as a single dose (0.5 ml) either SC or IM.

According to current practice, deployment of YF vaccine through preventive mass vaccination campaigns is recommended for target groups in areas at risk of YF where there is low vaccination coverage. Vaccination should be provided to everyone aged ≥ 9 months, in any area with reported cases. As YF vaccine is a live attenuated viral vaccine, a risk-benefit assessment should be undertaken for all pregnant and lactating women\textsuperscript{xix}. YF vaccine can be administered simultaneously with other vaccines.

**Fractional-dose vaccine administration**

For ease of implementation, a dose-sparing approach for YF vaccine should preferentially keep the same mode of delivery as for routinely used vaccine in the country, using traditional injection equipment. A fractional dose approach should consist of administration of a volume of not less than 0.1 ml using the standard SC or IM route of administration. Injection of a smaller volume of vaccine leads to difficulties such as oozing/loss of volume at injection site, limited availability of appropriately graduated auto-disable syringes, etc.

It is not advised to achieve dose sparing by diluting the vaccine with a larger volume than recommended by the manufacturer while maintaining a 0.5ml inoculum, due to programmatic and safety concerns.

If fractional dosing of YF is to be adopted, it is recommended that the dose should be administered using the same technique to which vaccinators are accustomed in their daily practice. Most of the injections

\textsuperscript{xviii} Adapted from https://extranet.who.int/gavi/PQ_Web/, accessed June 2016

\textsuperscript{xix} WHO Position Paper June 2013: Vaccines and vaccination against yellow fever (available at http://www.who.int/wer/2013/wer8827.pdf?ua=1, accessed June 2016)
provided through the immunization programmes are administered by IM or SC injection. For more information on experience in routine immunization programmes with delivering vaccines by the ID route see Annex 5. For Stamaril® (Sanofi), a programme may opt to administer the vaccine via the ID route, which is off-label, if the personnel are experienced in the administering via this route; otherwise, this vaccine should be administered by the SC route.

Wastage
Since opened vials of YF vaccine should usually be discarded no later than 6 hours (50-dose vial requires discarding after only 4 hours) after opening or at the end of the immunization session, whichever comes first, fractional dose administration could theoretically increase wastage. Data from YF mass vaccination campaigns indicate a 5% wastage rate (similar to measles and rubella vaccine campaigns that have similar handling characteristics) for 10-dose or 20-dose vials. This rate is significantly smaller than the indicative wastage rates for routine immunization. As 2-dose and 50-dose vials are not generally available and 5-dose vials are reserved for routine immunization, typically 10-dose vials are considered for use in vaccination campaigns.

Consequently, it could be expected that the administration of YF vaccination through wide age range campaigns could result in an effective use of the multidose vials, even the larger presentations, if the following factors are considered:

- Different vial presentation in densely populated/urban and rural settings: larger vials to be used in densely populated or urban settings.
- Different vial presentation for different age groups: some of the countries at risk have very young populations, e.g. Angola’s population is one of the youngest in the African continent, with nearly half of the population under 15 years of age. School (primary and secondary) based vaccination could target large numbers of children and support the use of larger vials.
- Timely reconstitution of the vaccine, based on the availability of the requisite number of patients.
- Training: for this aspect see section below.

Global supply of injection devices
Implementation of fractional-dose use of vaccines would entail a major increase in the use of injection devices with a smaller volume than those used with the full dose. Dose fractioning strategies must therefore be based on sufficient availability of suitable injection devices.

WHO is exploring availability of vaccines with various manufacturers for potential use in emergency campaigns in Angola and DRC.

Vaccine management and handling
Currently, the vial presentations of WHO prequalified YF vaccines are 2, 5, 10 and 20 doses. If used in a 1/2 dose approach, this represents the equivalent of 4, 10, 20 and 40 dose vials, and for a 1/5th fractional-dose approach (0.1ml) to the equivalent of 10, 25, 50 and 100 dose vials. Clearly from a practical standpoint, and given their availability and current information on the stopper, 10-dose vials are the best-available choice for mass campaigns (rapid consumption).
Several countries’ experiences with implementation of wide age-range supplementary immunization activities demonstrate that administration of YF vaccination using multidose vials – even of larger presentation – could be effective provided the factors concerning wastage are considered.

Since most opened vials of YF vaccine should be discarded 6 hours after opening or at the end of the immunization session (whichever comes first), use of fractional dose administration could increase wastage levels if large multidose vials are used. This is also borne out by estimations for measles and rubella supplemental immunization activities (SIAs), using a lyophilised vaccine with similar handling characteristics post-reconstitution to those of YF vaccine.

The question of whether multiple piercings of the rubber seal (septum) affects the integrity of the seal may need to be considered. As YF vaccine contains no preservative there is a potential increased risk of contamination if vials are repeatedly used (punctured) over the course of an immunization session. The use of lower dose vials would limit the number of punctures and reduce the risk of contamination. xx

Communication strategy
The development of a funded communication strategy and proper messaging on the new delivery approach (or technology) would be crucial to ensure health worker and community acceptance. This strategy would need to be developed by the Ministry of Health with adequate lead time, and would need to clearly justify and explain the updated approach adopted for mass vaccination. It is essential that the health workforce and general population do not equate fractional dosing with partial efficacy, which could jeopardize the credibility of the entire immunization programme.

Increased pain and swelling due to ID administration is a real risk, which may lead to lower public acceptance, decreased trust and therefore lower coverage in certain communities. These risks can be addressed by adequate training but programme communications on what to expect are key to community acceptance. The communication strategy should therefore include a component on crisis management and an effective response to adverse events that may occur following vaccination.

Health worker capacity building and training
All health personnel affected by the new strategy would need to be identified in order to be properly informed and adequately trained, particularly as this would be an off-label use of the vaccine. Health workers will need to be properly informed on this and more generally trained on aspects related to YF mass vaccination campaignsxxi. Depending on the administration technique chosen (ID or SC), appropriate training materials or guidance will need to be developed, which should also include all relevant aspects on safety and vaccine management, specifically adapted for the vaccine/manufacturer

xx PATH is currently planning to conduct this type of testing for IPV vials (ID IPV delivery) and potentially it could expand the testing to include yellow fever vials.

of choice and to the injection device to be used. Training is needed for health workers to identify how to calibrate the correct dose, as similar types of syringes may have more than one interpretable scale. If different syringes are supplied over time, this may create future confusion in the programme. Training and job aides should include all relevant aspects on vaccine handling, vaccination strategy and programme safety. Proper recording of vaccinations and monitoring should also be included in the training.

Adequate and sustained supervision would be essential for the successful implementation and monitoring of this approach and the activities should be included in the budget. As with any newly-introduced, unfamiliar practice, post-training support will be important and there will be a need to revise supervision instruments (tally sheets, monitoring forms may need to be adjusted) and develop feedback mechanisms. Supervision activities following initial training should be adequately planned and budgeted.

11. Surveillance and monitoring

Surveillance
When administering vaccination using a fractional dose within a campaign, individual vaccination records need to be established to allow for assessment of duration of protection, effectiveness, tracking of break-through cases and fractional dose vaccine safety (in particular rare SAEs following immunization, such as neurotropic and viscerotropic disease) according to age and closeness to the vial expiry date.

A YF Laboratory Network (YFLN) has been developed in the African Region based on the framework of the existing Global Measles-Rubella Laboratory Network (GMRLN). Currently, 24 National YF laboratories have been established in 21 Member States of the African Region, mainly in countries at risk for YF outbreaks. These National Laboratories have been established predominantly in already existing National Measles-Rubella Laboratories in order to benefit from the investments made by WHO to establish these MR laboratories. Investments were made in capacity building (including training in conducting IgM testing, QA/QC, biosafety, laboratory management) as well as provision of essential equipment (ELISA washer and reader, automatic pipettes).

According to the YF case definition, the diagnosis of a suspected case is confirmed by positive genome detection (PCR) or the detection of YF specific IgM that is negative for other flaviviruses (e.g. dengue, West Nile, or Zika viruses) by plaque reduction neutralization test (PRNT). Of note, YF specific IgM antibodies that are formed in response to infection with YF virus or to YF vaccine virus cannot be differentiated with currently available rapid diagnostic tests. Furthermore, YF IgM can persist for years following receipt of YF vaccine and therefore all suspect cases of YF vaccine should be asked about their previous history of YF vaccination in order to appropriately interpret the results.

WHO is working closely together with the Global Specialized Laboratory for YF at the Arbovirus laboratory, CDC-Fort Collins, USA, which routinely provides the network with essential reagents to
conduct YF IgM testing using a protocol developed by CDC and rolled out throughout the global laboratory network (LabNet). CDC also has a role in upgrading the expertise of individual laboratories and conducts referral testing, as well as quality assurance. A Regional Reference Laboratory (RRL) for the African Region has been established at the Institut Pasteur, Dakar, Senegal which provides confirmation of the results from national laboratories and further characterization of virus strains (IgM, IgG, virus isolation, molecular detection and characterization, virus neutralization) and QA/QC. This multi-tiered structure follows that of both GMRLN and GPLN (Global Polio LabNet).

As part of its guidance to the YFLN, WHO has published a laboratory manual for YF diagnosis\textsuperscript{xxii}. During the last 15 years, WHO has organized several laboratory-training workshops to strengthen skills of the YF laboratory staff. In addition, annual YFLN meetings are conducted jointly with polio and measles networks to share and benefit from their experience and highlight the integrated LabNet approach that WHO is striving for.

Currently, efforts are underway to strengthen laboratory capacity for YF testing in countries not previously dealing with YF transmission, and establishment of additional RRLs is being considered to relieve the workload of the Institut Pasteur in Dakar.

The integrated approach for YF with polio and measles diagnosis is also reflected in the integrated approach for YF surveillance.

**Monitoring**

A new WHO guideline *Planning and Implementing High Quality Supplementary Immunization Activities for Measles-Rubella and other Injectable Vaccines* has recently been developed.\textsuperscript{xxiii} The principles of campaign planning, implementation and monitoring recommended for measles-rubella vaccine can also be applied to mass YF vaccination campaigns. The guidelines are intended for use by immunization programme managers and their partners and provide tools for use before (i.e. readiness assessment), during (i.e. rapid convenience monitoring) and after (i.e. rapid convenience monitoring and mopping up and coverage surveys) the campaign.

Recording vaccinations administered during campaigns on a vaccination card/home-based health record is essential for the valid verification of immunization coverage during post-campaigns surveys, and for determining the total number of vaccine doses received by a child at school entry (where school enrolment screening policies exist). In particular for fractional dose use, personalized registries may prove useful when considering the need for revaccination with the full dose. Although the use of immunization cards can increase the campaign cost and workload, appropriate recording of every vaccination, fractional or full dose, (including those given during campaigns) is recommended by


WHO. Training and supervision will need to constantly reinforce this issue because in many countries cards are not marked during measles or measles/rubella SIAs or polio national immunization days.

It is also important to note that a recorded receipt of a fractional dose does not constitute a YF vaccination certificate as stipulated in the IHR.

12. Ethical considerations
In emergencies the international community has a collective duty of care to ensure that effective affordable measures are available to those most in need. The duty of care principle demands that effective vaccinations against disease threats should be available to those at risk. Emergencies often require rapid decision-making under uncertain and unconventional situations, but ethical principles need to be adhered to even in these situations.

In the face of shortages, a usual strategy is prioritization among different population groups. Another is to use a dose-sparing approach in order to cover as much of the population as possible. Both options could also be combined. The best of these options should be chosen based on a rigorous public health and ethical analysis.

A number of ethical issues arise when choosing a dose-sparing approach:

Risk-benefit considerations
First, the risk of harm to populations and individuals needs to be analysed (the ‘first do no harm’ principle). These risks and possible mitigating actions to minimize them should be explicitly discussed. Second, there should be robust evidence for benefit, i.e. for non-inferiority in comparison to the full dose. In addition, the dose-sparing strategy should be considered based on robust evidence for its benefit.

The obligation to produce and share data
In public health emergencies there is an ethical duty to produce and rapidly share all relevant data. The use of lower doses of vaccine as an emergency measure entails an ethical obligation to learn as much as possible as quickly as possible. Even if the dose-sparing approach is not designed as a research project, research components should be embedded to use this opportunity to gain new knowledge. Ideally, protocols should be submitted for pre-approval so that the final ethics review can be expedited.

Distributive justice and equity
Unless there is scientific necessity and evidence for doing so (e.g. based on safety or futility), the immunization programmes should not discriminate against any population groups. Special measures should be taken to facilitate the access of vulnerable groups, such as children and pregnant women.

**Transparency, trust, public engagement**
The vaccination strategy should be well communicated by national policy-makers to the public health officials, the public and the media. Special effort should be made to ensure that media understand well the rationale for the dose sparing strategy and become real partners in disseminating the messages of the vaccine programmes. Public engagement will facilitate uptake and trust in the programme.

**Informed consent**
During mass vaccination campaigns, consent is normally presumed (implicit consent), with a possibility to opt out. This means that information about the vaccine must be disseminated widely in an accessible format, and that it is ensured that members of the public know that they can opt out of vaccination, if they so wish. If mass vaccination campaigns are being planned with the lower-dose vaccine, it is an ethical requirement to provide minimum additional information, i.e. that a lower than usual dose will be used but that it is considered as safe and effective as the normal dose.
13. Recommendations

1. Fractional dose YF vaccination, an off-label use of the product, should be considered in response to an emergency situation in which current vaccine supply is insufficient. Fractional dose vaccination should be used for vaccination campaigns in response to an outbreak or in settings where the extension of the outbreak is imminent and should not be used for routine immunization. As soon as the vaccine supply situation normalizes, fractional dose should be replaced by full dose vaccination. Fractional dose vaccination is an off-label use of the product.

2. Under no circumstances should YF vaccine be reconstituted in a different volume of diluent than that recommended by the manufacturer, and no other method of diluting the vaccine should be used.

3. When fractional dose YF vaccine is used, preference should be given to the administration of the vaccine according to standard route, i.e. SC or IM. The minimal dose administered should preferentially contain 3000 IU/dose, but no less than 1000 IU/dose and the minimum volume of the inoculum should be not less than 0.1 ml.

4. The dose fractioning (e.g. 1/2 or 1/5th) should be done considering the potency of the vaccine batch, the shortage of supply and availability of suitable injection devices.

5. In the absence of data on the use of fractional dose YF vaccination in young children, children aged less than 2 years should preferentially be offered a full dose of vaccine (i.e. at least 3000 IU) during emergency campaigns.

6. Different expansion scenarios for YF vaccine fractional dose administration should be considered in view of the potential risk of further spread of the disease, and shortage of vaccine supply. Actual potencies of available vaccines need to be considered to meet the necessary potency levels:
   a. 1/2 dose of Bio-Manguinhos vaccine administered SC.
   b. Should the shortage of vaccine limit the use of a 1/2 dose, use of a 1/5th dose of Bio-Manguinhos vaccine administered SC could be considered.
   c. If the shortage limits fractional dose supplies, all WHO prequalified vaccines could be administered as 1/2 or 1/5th fractional dose SC, depending on potency of the batch. In this context, use of Stamaril ® (Sanofi) via ID administration (0.1.ml) is, while off-label, also acceptable, depending on the preferences of the country. As a general rule, fractional doses should not be less than the minimal dose range (see recommendation 3).

7. Reconstituted YF vaccine is heat labile and must be kept at 2–8 °C at all times and discarded after 6 hours in accordance with WHO’s open vial policy.

8. Multidose vials containing more than 10 full doses should not be used for fractional dose administration in order to avoid increased risk of contamination due to multiple punctures of the septum.
9. Every effort should be made to monitor safety and YF vaccine AEFIs.

10. Vaccination with fractional doses should be recorded using personalized registries for the purpose of safety and effectiveness monitoring. Such information may prove useful in assessing eventual re-vaccination needs with full doses, for which currently there is no recommendation.

11. All other precautions and recommendations for YF vaccination remain valid as detailed in the WHO yellow fever vaccine position paper (2013).

14. Research needs

The currently available data appear sufficiently strong for emergency policy decision-making on use of the YF vaccines from two manufacturers (Sanofi Pasteur and Bio-Manguinhos) with fractional dose administration by ID and IM/SC injection, respectively. However, to support a broader recommendation on fractional dose use of YF vaccine, additional data are needed and ideally all 4 WHO prequalified YF vaccines should be studied. Furthermore, since the data on fractional doses were generated in adult study populations, there is an urgent need to compile clinical trial data in children and infants. The specific research needs include the following:-

- Immunological non-inferiority trials should be conducted to compare the full dose vs. a fractional dose of \( \frac{1}{2} \) (0.25ml) and \( \frac{1}{5} \)th of the volume (0.1ml) using the same route of administration for all prequalified vaccines;
- Vaccine should include lots ex-factory and end of shelf-life, with recently measured potency expressed in IU.
- Studies should be conducted in healthy adults in flavivirus-naïve subjects, and with representative background of flavivirus pre-existing immunity, which should be duly characterized (dengue, YF, Zika, WNV in priority).
- An age de-escalation study should be conducted in children down to 9 months in order to assess immunogenicity.
- All studies should report baseline immune status, measure YF functional antibodies at 28 days and 12 months after vaccination using validated PRNT; viraemia (adults only), and safety and reactogenicity using standard procedures;
- Measures should be put in place for long-term follow up of vaccinated subjects, and booster vaccination should be offered in case titres may fall below the protective threshold.

15. Annexes

Annex 1: Search strategies for the use of yellow fever vaccine for IM/SC delivery

Search engine: PubMed
Search term: “yellow fever vaccine” and (“fractional dose*” or “dose-sparing” or “dose sparing” or “subdose*”)

Language: no limitation
Period: no limitation

Result: only 1 study (= study#4 was identified)

The other 2 studies (study#1 and #3 were identified by the references of study#4)

**Search strategies for the use of yellow fever vaccine for intradermal delivery**

Search engine: PubMed

Search term: “yellow fever vaccine” and “intradermal”

Language: no limitation

Period: no limitation

Result: Of 5 articles identified, 2 articles were dose-sparing related studies; 1 study is study#2 of this review. Another study identified from the review was excluded because (i) sample number was only 7, and (ii) target population was only persons with egg allergy.
Annex 2: GRADE tables

GRADE table 1 on the use of a fractional dose 17DD YF vaccine (1/5th of full dose) via regular route of administration

**Population**: Immunocompetent individuals  
**Intervention**: Fractional dose 17DD YF vaccine with 1/5th of 0.5ml (full dose) SC/IM within a YF vaccination campaign  
**Comparison**: Full dose of 17DD YF vaccine  
**Outcome**: Cases of YF in outbreak settings

| In immunocompetent individuals, does a fractional dose (1/5th of full dose (0.5ml)) administered via regular route of administration prevent YF disease? |
|---|---|---|
| Rating | Adjustment to rating |
| No. of studies/starting rating | 1/RCT 2/Observational | 4 |
| Limitation in study design | Serious**xxv** | -1 |
| Inconsistency | None serious | 0 |
| Indirectness | Serious**xxvi** | -1 |
| Imprecision | Not serious | 0 |
| Publication bias | None serious | 0 |
| Large effect | Not applicable | 0 |
| Dose-response | Not applicable | 0 |
| Antagonistic bias and confounding | Not applicable | 0 |
| Final numerical rating of quality of evidence | 2 |

**Summary of Findings**

**Statement on quality of evidence**: Evidence supports a limited level of confidence that the true effect lies close to that of the estimate of the effect on the health outcome.

**Conclusion**: In outbreak setting, using a fractional dose of 17DD YF vaccine via regular route of administration in vaccination campaign may be warranted to mitigate the risk of YF disease and discontinue further spread of the virus despite limited confidence in the quality of the evidence.

**References**


**xxv** No allocation concealment reported.

**xxvi** Administered to healthy male volunteers only; Immunogenicity data only; Study results stem from one WHO prequalified YF vaccine and might not be extrapolated to the other WHO prequalified vaccines; Potency of the vaccine may vary by batch and time of administration.
GRADE table 2 on the use of a fractional dose 17D YF vaccine (1/5\textsuperscript{th} of full dose) administered intradermally

**Population**: Immunocompetent individuals  
**Intervention**: Fractional dose 17DD YF vaccine with 1/5\textsuperscript{th} of 0.5mL (full dose) SC/IM within a YF vaccination campaign  
**Comparison**: Full dose of 17DD YF vaccine  
**Outcome**: Cases of YF in outbreak settings

In immunocompetent individuals, does a fractional dose (1/5\textsuperscript{th} of full dose (0.5ml)) administered intradermally prevent YF disease?

<table>
<thead>
<tr>
<th>Factors decreasing confidence</th>
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<th>Adjustment to rating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Limitation in study design</td>
<td>Serious\textsuperscript{xxvi}</td>
<td>-1</td>
</tr>
<tr>
<td>Inconsistency</td>
<td>None serious</td>
<td>0</td>
</tr>
<tr>
<td>Indirectness</td>
<td>Serious\textsuperscript{xxviii}</td>
<td>-1</td>
</tr>
<tr>
<td>Imprecision</td>
<td>Not serious</td>
<td>0</td>
</tr>
<tr>
<td>Publication bias</td>
<td>None serious</td>
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</table>

<table>
<thead>
<tr>
<th>Factors increasing confidence</th>
<th>Rating</th>
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<tbody>
<tr>
<td>Large effect</td>
<td>Not applicable</td>
<td>0</td>
</tr>
<tr>
<td>Dose-response</td>
<td>Not applicable</td>
<td>0</td>
</tr>
<tr>
<td>Antagonistic bias and confounding</td>
<td>Not applicable</td>
<td>0</td>
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</tbody>
</table>

Final numerical rating of quality of evidence: 2

**Summary of Findings**

**Statement on quality of evidence**: Evidence supports a limited level of confidence that the true effect lies close to that of the estimate of the effect on the health outcome

**Conclusion**: In outbreak setting, using a fractional dose of 17D YF vaccine ID in vaccination campaign may be warranted to mitigate the risk of YF disease and discontinue further spread of the virus despite limited confidence in the quality of the evidence.

**References**

1. Roukens A. Intradermally Administered Yellow Fever Vaccine at Reduced Dose Induces a Protective Immune Response: A Randomized Controlled Non-Inferiority Trial. Volume 3, Issue 4, Plos One 2008

\textsuperscript{xxvi} No blinding of participants.  
\textsuperscript{xxvii} Study results stem from one WHO prequalified YF vaccine and might not be extrapolated to the other WHO prequalified vaccines; Potency of the vaccine may vary by batch and time of administration.
Annex 3: Risk of bias assessment using Cochrane Collaboration’s tool

Campi-Azevedo AC et al. 2014

Methods
Randomized controlled trial

Participants
900 healthy male volunteers (mean age 19.4 years) from military units in Rio de Janeiro, Brazil

Interventions
Full dose of yellow fever vaccine and five lower alternative formulations (Bio-Manguinhos)

Outcomes
Neutralizing antibody titres, viraemia, cytokines and chemokines.

Notes

Risk of bias table

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Not reported.</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Not reported.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Unclear risk</td>
<td>Not reported.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>Not reported.</td>
</tr>
</tbody>
</table>
Incomplete outcome data (attrition bias)

Unclear risk

Unclear risk

Unclear risk

Unclear risk

Unclear risk

Unclear risk

Not reported.

Selective reporting (reporting bias)

Unclear risk

Unclear risk

Unclear risk

Unclear risk

Unclear risk

Not reported.

Other bias

Unclear risk

Unclear risk

Unclear risk

Unclear risk

Unclear risk

Lopes O et al. 1988

Methods
Observational study

Participants
300 healthy male volunteers from military units in Rio de Janeiro, Brazil. Age range: 18-47 years (Mean 21.7 years).

Interventions
Yellow fever vaccine administered at different dilutions (Undiluted; 1:10; 1:60; 1:100, 1:1000)

Outcomes
Immunogenicity; Adverse events following immunization.

Notes

Risk of bias table

Bias

Authors' judgement
Support for judgement

Random sequence generation (selection bias)
High risk
Participants were allocated to each vaccine group in the order they reported for inoculation.

Allocation concealment (selection bias)
High risk
No reported allocation concealment.
Martins RM et al. 2013

Methods
Randomized controlled trial

Participants
900 healthy male volunteers (mean age 19.4 years) from military units in Rio de Janeiro, Brazil

Interventions
Full dose of yellow fever vaccine and five lower alternative formulations
Outcomes

Seroconversion, and neutralizing antibodies geometric mean titre; Adverse events following immunization

Notes

Risk of bias table

<table>
<thead>
<tr>
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<th>Authors' judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
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<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Not reported.</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Not reported.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>Unclear risk</td>
<td>Participants and personnel were blinded.</td>
</tr>
<tr>
<td>Blinding of outcome assessment (detection bias)</td>
<td>Unclear risk</td>
<td>Self-reporting of adverse reactions following immunization</td>
</tr>
<tr>
<td>Incomplete outcome data (attrition bias)</td>
<td>Unclear risk</td>
<td>First and last blood sample obtained from all volunteers, 2nd blood sample obtained from 85.6% of volunteers.</td>
</tr>
<tr>
<td>Selective reporting (reporting bias)</td>
<td>Unclear risk</td>
<td>Unclear whether any outcomes were measured but not reported based on the results</td>
</tr>
</tbody>
</table>
### Roukens AH et al. 2008

#### Methods
Randomized controlled non-inferiority trial

#### Participants
Healthy volunteers (18 years and older) 155 primary vaccinees and 20 revaccinees

#### Interventions
Intradermal 0.1ml yellow fever vaccine; 0.5ml yellow fever vaccine subcutaneously (Sanofi)

#### Outcomes
Immunogenicity; adverse events following immunization.

#### Notes

<table>
<thead>
<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Random sequence generation (selection bias)</td>
<td>Unclear risk</td>
<td>Randomization by the investigator using permuted-block randomization.</td>
</tr>
<tr>
<td>Allocation concealment (selection bias)</td>
<td>Unclear risk</td>
<td>Treatment allocation was concealed in sealed envelopes.</td>
</tr>
<tr>
<td>Blinding of participants and personnel (performance bias)</td>
<td>High risk</td>
<td>Participants could identify to which group they were allocated to by location of vaccination and type of syringe used.</td>
</tr>
<tr>
<td>Bias</td>
<td>Risk Level</td>
<td>Description</td>
</tr>
<tr>
<td>------------------------------------</td>
<td>------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Blinding of outcome assessment</td>
<td>Unclear</td>
<td>Self-reported adverse reactions following immunization documented by participants during 3 weeks after immunization who were blind to treatment allocation.</td>
</tr>
<tr>
<td>Incomplete outcome data</td>
<td>Low</td>
<td>Participants completed outcomes assessment.</td>
</tr>
<tr>
<td>Selective reporting</td>
<td>Unclear</td>
<td>Unclear whether any outcomes were measured but not reported based on the results.</td>
</tr>
<tr>
<td>Other bias</td>
<td>Unclear</td>
<td>No other sources of bias identified.</td>
</tr>
</tbody>
</table>
**Annex 4: Evidence-to-recommendation table (draft table, to be completed after more data/recommendations are available)**

**Question**: In immunocompetent individuals, should a fractional dose (1/2 or 1/5th of full dose (0.5ml)) of YF vaccine be administered in case of YF vaccine supply shortages?

**Population**: Immunocompetent individuals in the context of the current yellow fever outbreak

**Intervention**: Dose-sparing strategies through fractional dosing of YF vaccine.

**Comparison(s)**: Continued use of full dose/ no vaccination.

**Outcome**: Individual short-term protection, containing of ongoing outbreak.

**Background**: Ongoing yellow fever outbreaks are sharply increasing the demand for YF vaccine, are exhausting the global stockpile and are putting at risk the immunization of endemic populations, and travellers to those countries for which YF vaccine is mandatory. Dose-sparing strategies through fractional dosing of YF vaccine may be promising in the context of the current outbreak. These dose-sparing strategies are assessed by the Strategic Advisory Group of Experts (SAGE) on Immunization.

<table>
<thead>
<tr>
<th>CRITERIA</th>
<th>JUDGEMENTS</th>
<th>RESEARCH EVIDENCE</th>
<th>ADDITIONAL INFORMATION</th>
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</thead>
<tbody>
<tr>
<td><strong>PROBLEM</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Is the problem a</strong></td>
<td>No</td>
<td>The current outbreak remains of great concern to WHO.</td>
<td></td>
</tr>
<tr>
<td>public health</td>
<td>Uncertain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>priority?</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Benefits of the</strong></td>
<td>No</td>
<td>Number of doses to be obtained by fractional dose use is double/ five-fold.</td>
<td></td>
</tr>
<tr>
<td><strong>intervention</strong></td>
<td>Uncertain</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Are the desirable</strong></td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>anticipated</td>
<td>Uncertain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>effects large?</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Harms of the</strong></td>
<td>No</td>
<td>Reactogenicity of a fractional dose is comparable to that of a full dose.</td>
<td></td>
</tr>
<tr>
<td><strong>intervention</strong></td>
<td>Uncertain</td>
<td>No risk of serious adverse events following immunization has been assessed.</td>
<td></td>
</tr>
<tr>
<td><strong>Are the</strong></td>
<td>Yes</td>
<td>Nevertheless, there may be programmatic safety considerations arising from the use</td>
<td></td>
</tr>
<tr>
<td>undesirable</td>
<td>Uncertain</td>
<td>of the fractional dose through multiple punctures of the rubber seal and consecutive</td>
<td></td>
</tr>
<tr>
<td>anticipated</td>
<td>Yes</td>
<td>contamination of the vial.</td>
<td></td>
</tr>
<tr>
<td>effects small?</td>
<td>Uncertain</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


### Balance between benefits and harms

<table>
<thead>
<tr>
<th>Favours intervention</th>
<th>Favours comparison</th>
<th>Favours both</th>
<th>Favours neither</th>
<th>Unclear</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td></td>
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</tbody>
</table>

Balancing the benefits and harms of the intervention and the risk of yellow fever disease within the context of the current outbreak, the intervention should be favoured.

### What is the overall quality of this evidence for the critical outcomes?

- No included studies
- Very low
- Low
- Moderate
- High

Quality of the available evidence on the use of the fractional dose is low due to study limitations and indirectness in terms of the target population of the trials (for further information, see the GRADE tables. Although no different table was done for the use of ½ dose of YF vaccine, the quality of this evidence is as for the 1/5 fractional dose SC, hence represents a possibility to use).

### VALUES & PREFERENCES

#### How certain is the relative importance of the desirable and undesirable outcomes?

- Important uncertainty or variability
- Possibly important uncertainty or variability
- Probably no important uncertainty or variability
- No important uncertainty or variability
- No known undesirable outcomes

No evidence available but the importance of the desirable and undesirable outcomes may vary within the target population.

#### Values and preferences of the target population: Are the desirable effects large relative to undesirable effects?

- No
- Probably No
- Uncertain
- Probably Yes
- Yes
- Varies

It is assumed that the values and preferences of the target population are in favour of the fractional dose to avoid the risk of acquiring the natural disease despite the potential harms associated with the fractional dose use.
<table>
<thead>
<tr>
<th>RESOURCE USE</th>
<th>Are the resources required small?</th>
<th>No</th>
<th>Uncertain</th>
<th>Yes</th>
<th>Varies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>No available evidence but resources may be relatively considerable for implementation of immunization campaigns and ensuring adequate social mobilization.</td>
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<td></td>
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<table>
<thead>
<tr>
<th>COST-EFFECTIVENESS</th>
<th>Cost-effectiveness</th>
<th>No</th>
<th>Uncertain</th>
<th>Yes</th>
<th>Varies</th>
</tr>
</thead>
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<tr>
<td></td>
<td></td>
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<td></td>
<td></td>
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<tr>
<td></td>
<td>No available evidence, but likely less of a priority in the context of the current public health threat.</td>
<td></td>
<td></td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>EQUITY</th>
<th>What would be the impact on health inequities?</th>
<th>Increased</th>
<th>Uncertain</th>
<th>Reduced</th>
<th>Varies</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>YF mainly affects poor populations in densely-populated urban slums. Implementation of a fractional dose may reduce health inequities.</td>
<td></td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>ACCEPTABILITY</th>
<th>Which option is acceptable to key stakeholders (Ministries of Health, Immunization Managers)?</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Both</th>
<th>Neither</th>
<th>Unclear</th>
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<tbody>
<tr>
<td></td>
<td>Intervention is likely to be acceptable to the stakeholders.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>ACCEPTABILITY</th>
<th>Which option is acceptable to target group?</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Both</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Intervention is likely to be acceptable to the target population.</td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>FEASIBILITY</th>
<th>Is the intervention feasible to implement?</th>
<th>No</th>
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<th>Uncertain</th>
<th>Probably Yes</th>
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</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>There may be programmatic challenges to implement the use of a fractional dose, but nevertheless the intervention is likely to be feasible.</td>
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<table>
<thead>
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<th>FEASIBILITY</th>
<th>Balance of consequences</th>
<th>Undesirable consequences</th>
<th>Undesirable consequences</th>
<th>The balance between desirable and undesirable consequences</th>
<th>Desirable consequences</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>clearly outweigh</td>
<td>desirable consequences</td>
<td>probably outweigh</td>
<td>is closely balanced or uncertain</td>
<td>probably outweigh</td>
</tr>
<tr>
<td></td>
<td>in most settings</td>
<td>in most settings</td>
<td>desirable consequences</td>
<td></td>
<td>undesirable consequences in most settings</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Desirable consequences</td>
<td>clearly outweigh</td>
<td>undesirable consequences in most settings</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

34
<table>
<thead>
<tr>
<th>Type of recommendation</th>
<th>We recommend the intervention</th>
<th>We suggest considering recommendation of the intervention</th>
<th>We recommend the comparison</th>
<th>We recommend against the intervention and the comparison</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Only in the context of rigorous research</td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Only with targeted monitoring and evaluation</td>
<td></td>
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<tr>
<td></td>
<td></td>
<td>Only in specific contexts or specific (sub)populations</td>
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| Recommendation (text) | 1. The use of YF fractional dose vaccination, which is an off-label use of the product, should be considered in response to an emergency situation in which current vaccine supply is insufficient. Fractional dose vaccination should be used for vaccination campaigns in response to an outbreak or in settings where the extension of the outbreak is imminent and should not be used for routine immunization. As soon as the vaccine supply situation normalizes, fractional dose should be replaced by full dose vaccination. Fractional dose vaccination is an off-label use of the product.
2. Under no circumstances should YF vaccine be reconstituted in different volume of diluent than that recommended by the manufacturer, and no dilution of the vaccine should be done by any other methods.
3. When YF vaccine is administered in fractional doses, preference should be given to the administration of the vaccine according to standard route, i.e. SC or IM. The minimal dose administered should preferentially contain 3000 IU/dose, but no less than 1000 IU/dose and the minimum volume of the inoculum should be not less than 0.1 ml.
4. The dose fractioning (1/2 or 1/5th) should be done considering the potency of the vaccine batch, the shortage of supply and availability of suitable injection devices.
5. In the absence of data on the use of fractional dose in young children, children below the age of 2 years should preferentially be offered a full dose of vaccine (i.e. at least 3000 IU) during emergency campaigns.
6. Different expansion scenarios for YF vaccine fractional dose administration should be considered in view of the anticipated risk of the spread of the disease, and shortage in vaccine supply. Actual potencies of available vaccines need to be considered to meet potency levels as discussed before:
   a. 1/2 dose of Bio-Manguinhos vaccine administered SC.
   b. Should the shortage of vaccine limit the use of 1/2 dose, use of a 1/5th dose of Bio-Manguinhos vaccine administered SC could be considered.
   c. If the shortage affects fractional dose supply, all WHO prequalified vaccines could be administered as 1/2 or 1/5th fractional dose SC, depending on potency of the batch. In such a context, use of Stamaril ® (Sanofi) via ID administration (0.1.ml) is, while off-label, also acceptable, depending on the preferences of the country. As a general rule, fractional doses should not be less than the recommended minimal dose range.
7. Reconstituted YF vaccine is heat labile and must be kept at 2–8 °C at all times and discarded after 6 hours in accordance with WHO’s open vial policy.
8. No multidose vials containing more than 10 full doses should be used for fractional dose administration in order to reduce risk of contamination through multiple punctures of the rubber seal (septum). |

| Implementation considerations | - No multi-dose vials containing more than 10 full doses should be used for fractional dose administration to reduce risk of contamination through multiple puncture of the septum.
- During the vaccination session every effort must be made to keep reconstituted vaccine cold.
- Appropriate syringes (0.1 ml AD syringes) must be used for vaccine administration.
Adequate communication and training of Health Care Workers is required. |
| Monitoring and evaluation | When administering vaccination as a fractional dose during a campaign, individual vaccination records need to be established to allow for assessment of duration of protection, effectiveness, tracking of break-through cases and fractional dose vaccine safety (in particular rare serious adverse events following immunization, such as neurotropic and viscerotropic disease) according to age and pending on closeness of the vials to expiry date. |
| Research priorities | The specific research needs include:  
- Immunological non-inferiority trials should be conducted comparing the full dose vs. a fractional dose of $\frac{1}{2}$ (0.25ml) and $\frac{1}{5}$th of the volume (0.1ml) using the same route of administration for all prequalified vaccines;  
- Vaccine should include lots ex-factory and end of shelf-live, with recently measured potency expressed in IU.  
- Studies should be conducted in healthy adults in flavivirus-naive subjects, and with representative background of flavivirus pre-existing immunity, which should be duly characterized (dengue, YF, Zika, WNV in priority).  
- An age de-escalation study should be conducted in children down to 9 months in order to assess immunogenicity.  
- All studies should report baseline immune status, measure YF functional antibodies D 28 and after 12 months using validated PRNT; viraemia (adults only), and safety and reactogenicity using standard procedures;  
- Measures should be put in place for long term follow-up of vaccinated subjects, and booster vaccination should be offered in case titres may fall below the protective threshold. |
Annex 5: Programme experience in routine immunization programmes with delivery of vaccines intradermally (ID)

Beyond administration of BCG, there is limited experience in routine immunization programmes with delivery of vaccines by the ID route, and particularly in a mass campaign setting. ID inoculation is a difficult field technique, and in a mass campaign setting would be particularly stressful for health workers to exercise confidently and with precision. Experience in Nigeria with BCG administration during child health days has reportedly been unsuccessful, leading to frustrated health workers and dissatisfaction or departure by clients due to long waiting times. Furthermore, incorrect administration may lead to unpleasant local reactions, as described in the injection safety section. Consequently, ID delivery of YF is the least preferable method from a programmatic perspective.

In early 2016, India began administering inactivated polio vaccine (IPV) fractional dose via ID delivery in 8 states, using BCG syringes, indicating that in higher performing programmes with skilled health workers, combined with adequate training, this approach is feasible in a routine setting. However, it is important to note that India has already implemented ID vaccination beyond BCG, administering rabies vaccination using insulin syringes. Monitoring of programme challenges and success are ongoing.

To understand the feasibility of ID vaccination for the administration of fractional dose (1/5th of full dose) IPV, the WHO Global Polio Eradication Initiative (GPEI) and PATH have clinically evaluated ID delivery technologies (PharmaJet Tropis disposable-syringe jet injector29, West Pharmaceutical Services’ ID Adapters30). In early 2017, these injectors for ID administration will become available for mass administration of IPV. However, the regulatory agency in the countries of manufacture might require an application for license of these injectors with a specific vaccine, in this case YF vaccine. Lead production times are expected to be around 10 months.

16. References


