

District guidelines for yellow fever surveillance



**DIVISION OF EMERGING AND OTHER COMMUNICABLE
DISEASES SURVEILLANCE AND CONTROL
GLOBAL PROGRAMME FOR VACCINES AND IMMUNIZATION
EXPANDED PROGRAMME ON IMMUNIZATION**



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List of abbreviations

EPI	Expanded Programme on Immunization of the World Health Organization
IgG	Immunoglobulin type G
IgM	Immunoglobulin type M
MOH	ministry of health
Nm	nanometre (10 ⁻⁹ m.)
RNA	Ribonucleic acid
YF	yellow fever

1. Introduction: yellow fever control and prevention

Yellow fever is a viral haemorrhagic fever transmitted by mosquitos infected with the yellow fever virus. The disease is untreatable, and case fatality rates in severe cases can exceed 50%.

Yellow fever can be prevented through immunization with the 17D yellow fever vaccine. The vaccine is safe, inexpensive and reliable. A single dose provides protection against the disease for at least 10 years and possibly life-long.

There is high risk for an explosive outbreak in an unimmunized population—and children are especially vulnerable—if even one laboratory-confirmed case of yellow fever occurs in the population. Effective activities for disease surveillance remain the best tool for prompt detection and response to an outbreak of yellow fever especially in populations where coverage rates for yellow fever vaccine are not high enough to provide protection against yellow fever.

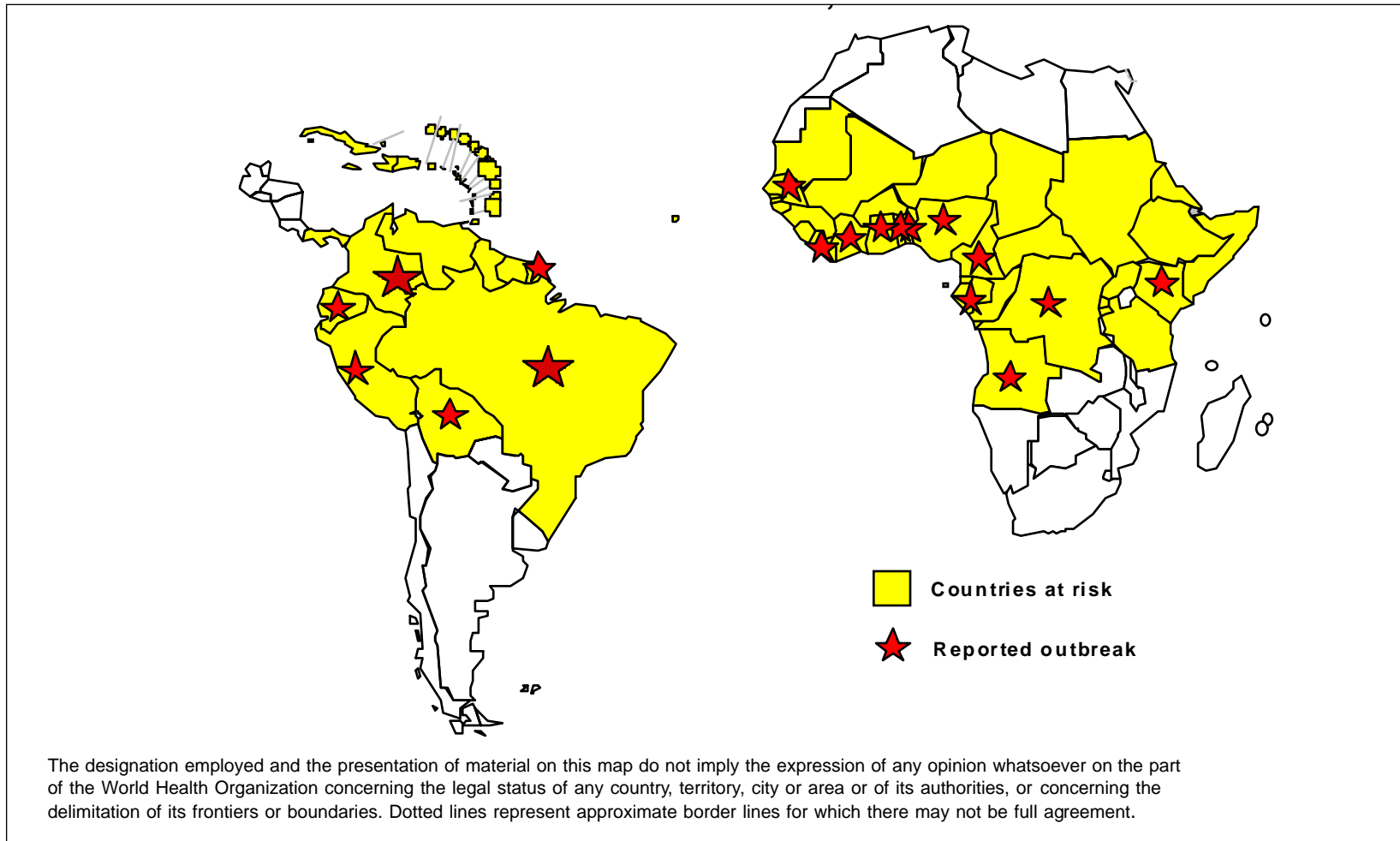
The guidelines in this manual describe how to detect and confirm suspected cases of yellow fever. They also describe how to respond to an outbreak of yellow fever and prevent additional cases from occurring. The guidelines are intended for use at the district level.

Yellow fever epidemiology

Yellow fever occurs most often in Africa and South America. The epidemiology of yellow fever presents different challenges on each continent, even though it is caused by the same virus. In South America, yellow fever mainly affects forest workers. In Africa, serious epidemics have affected unimmunized populations in rural and urban areas. African and South American cities have the potential for epidemics if the *Aedes aegypti* mosquito, a species of mosquito that carries the yellow fever virus, is found in densely populated areas.

There has been an increase in the number of reported yellow fever cases in Africa during the last five to ten years. WHO estimates 200 000 yellow fever cases now occur each year, with an estimated 30 000 deaths in 34 at-risk countries, almost all of them in sub-Saharan Africa. Causes for the increase are probably due to reduced coverage rates for yellow fever immunizations and abandonment of mosquito-control programmes. The movement of people from rural to urban areas has resulted in large numbers of people living in conditions of poverty, crowded housing and poor sanitation. These conditions amplify the risk for yellow fever transmission.

Figure 1: Countries at risk for yellow fever and having reported at least one outbreak, 1985-1998



The precise extent of illness and death due to yellow fever is not known. Estimates by WHO and other international agencies suggest that only one to two per cent of the cases are actually reported. An outbreak of yellow fever can go undetected because the signs and symptoms of yellow fever are similar to viral hepatitis, malaria, leptospirosis, typhus, Ebola haemorrhagic fever and other viral haemorrhagic fevers. It is difficult for health workers to make a definitive diagnosis based on the signs and symptoms alone. And, mild cases can go undetected because the patient is likely to be treated at home and does not seek care in a health facility.

The yellow fever virus, its natural hosts and vectors

- The **agent** that causes yellow fever is a virus that belongs to the *Flavivirus* genus, a large group of RNA viruses. The yellow fever virus is 35-40 nm in size. It consists of a single strand of RNA and protein nucleocapsid surrounded with a lipid envelope.
- The **natural host** for the yellow fever virus in forest areas is non-human primates (usually monkeys and chimpanzees).
- The **vectors** of yellow fever in forest areas in Africa are *Aedes africanus*, and other *Aedes* species. In South America, the primary vector is the *Haemagogus* species. In urban areas of both Africa and South America, the vector is *Aedes aegypti*.

Clinical features of yellow fever

Yellow fever presents with a variety of clinical signs and outcomes ranging from mild to severe and fatal cases. Yellow fever in human beings has the following characteristics:

- An **acute phase** lasting for four to five days and presenting with:
 - a sudden onset of fever
 - headache or backache
 - muscle pain
 - nausea
 - vomiting
 - red eyes (infected conjunctiva).

This phase of yellow fever can be confused with other diseases that also present with fever, headache, nausea and vomiting because jaundice may not be present in less severe (or mild) cases of yellow fever. The less severe cases are often non-fatal.

- A temporary **period of remission** follows the acute phase in 5% to 20% of cases. The period of remission lasts for up to 24 hours.

-
- A **toxic phase** can follow the period of remission and presents with:
 - jaundice
 - dark urine
 - reduced amounts of urine production
 - bleeding from the gums, nose or in the stool
 - vomiting blood
 - hiccups
 - diarrhoea
 - slow pulse in relation to fever

No specific treatment is available for yellow fever. In the toxic phase, supportive treatment includes therapies for treating dehydration and fever. In severe cases, death can occur between the seventh and tenth days after onset of the first symptoms.

Laboratory analysis of blood or tissue samples (usually liver) is needed to confirm a case of yellow fever. The analysis requires special reagents and techniques for measuring the presence of IgM and IgG antibodies or for isolating the virus from the blood or tissue sample. **Note: Liver samples are taken from fatal cases only.**

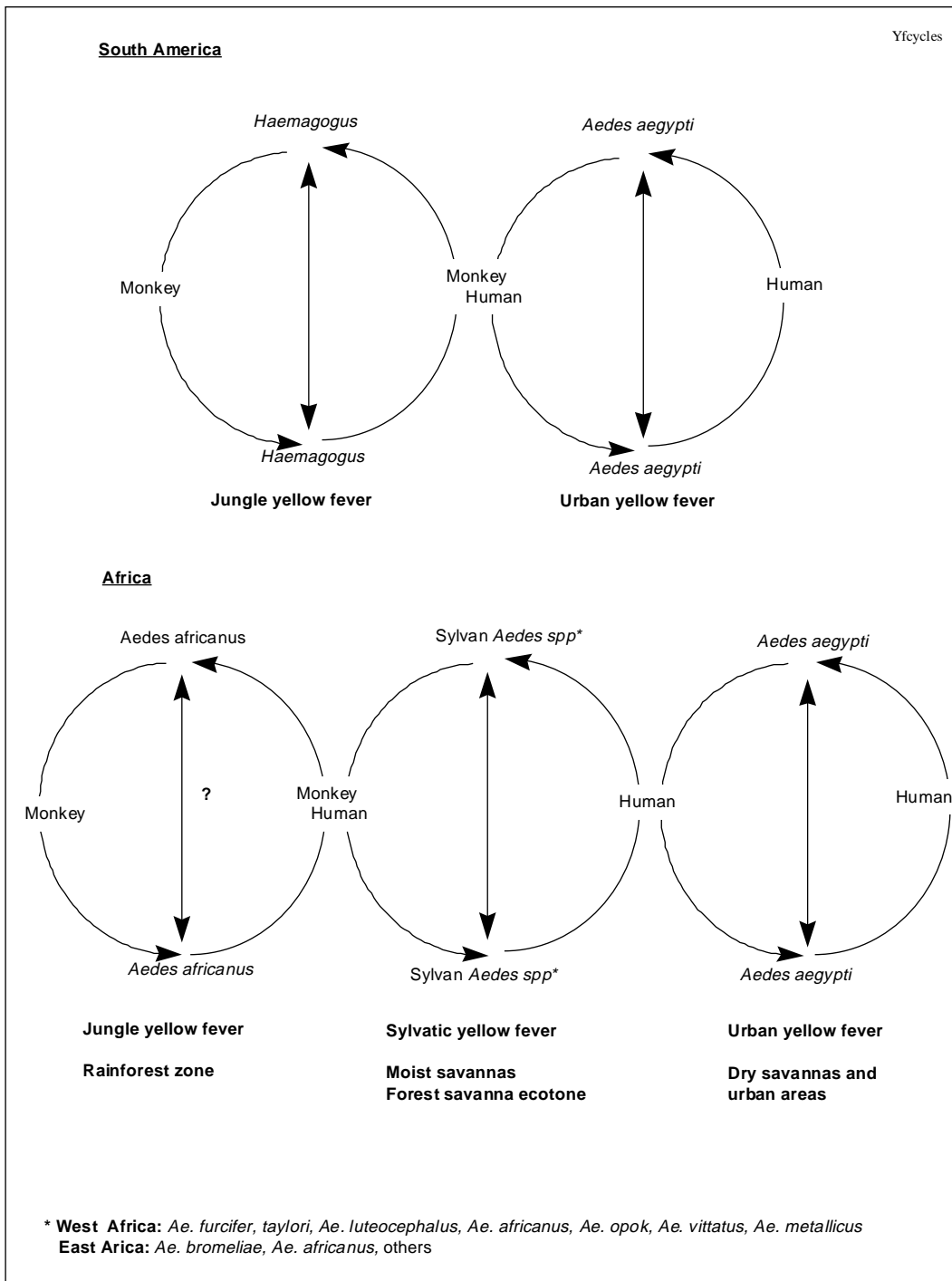
Transmission of yellow fever

Yellow fever is transmitted to humans when they are bitten by mosquitos infected with the yellow fever virus. The incubation period is three to seven days. Mosquitos are infected by feeding on patients in the first three to four days of illness, the time when the virus is circulating in the blood.

The yellow fever virus is transmitted in both forest and urban cycles.

- In the **forest cycle**, the yellow fever virus lives in mosquito species (*Aedes africanus*, *Haemagogus* species and others) that breed in tree holes. The disease is transmitted among monkeys and other small primates. Humans become infected when they enter the forest and are bitten by a mosquito carrying the yellow fever virus. Where sylvatic vectors are present at high density, such as in the savannah zone of Africa, humans may serve as the principal host in epidemic transmission.
- In an **urban cycle**, an infected domestic mosquito, *Aedes aegypti*, transmits the virus from human to human. When a case is undetected, there is potential for an epidemic.

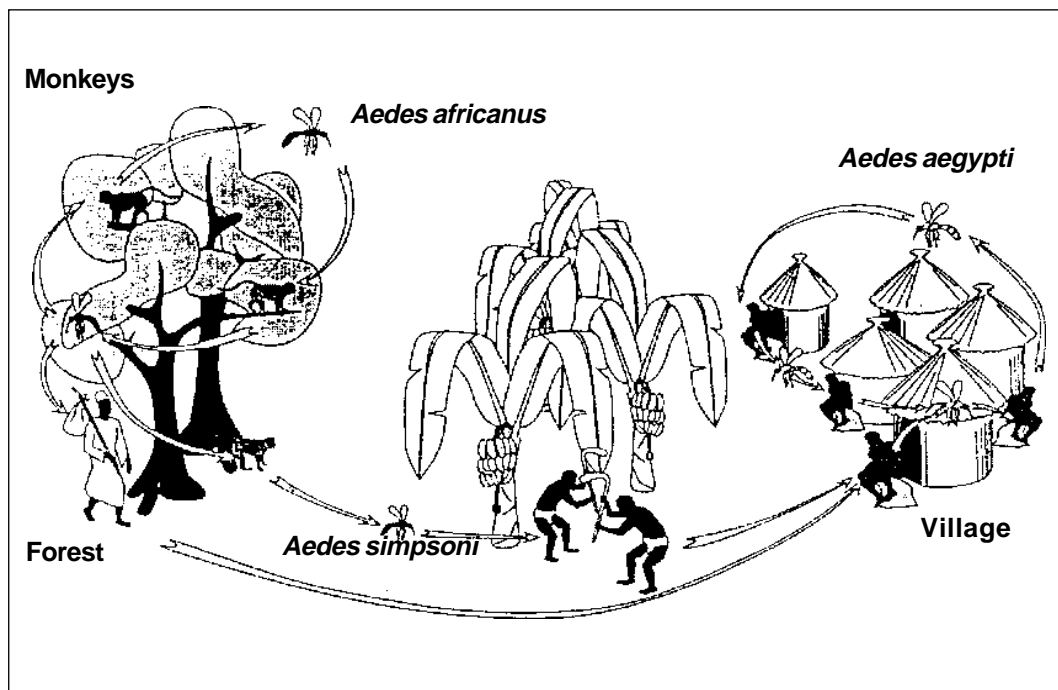
Figure 2: Transmission cycles



Generally, the transmission patterns involve the following geographic boundaries or “transmission zones.”

- **Endemic zones** are areas where the yellow fever virus is continuously present on an enzootic basis. These zones include forest areas where the yellow fever virus circulates between mosquitos and monkeys or chimpanzees.
- An **intermediate or emergence zone** is any area next to or outside an endemic zone that includes domestic human activity such as villages, farm land, and herding areas. There is increased potential for human-to-human transmission in this zone when yellow fever-infected mosquitos from the endemic zone lay their eggs in fields or savannahs outside the forest area. The virus remains dormant in the mosquito eggs throughout the dry season and emerges in the rainy season. Humans working or living in the fields or savannah can become infected when they are bitten by the infected mosquitos.
- A **high risk area** is an area where there is potential for an epidemic because a human infected with yellow fever has been bitten by the *Aedes aegypti* mosquito. As a result, the mosquito becomes a vector for the yellow fever virus. The mosquito spreads yellow fever when it bites non-infected humans. This establishes human-to-human transmission, and the conditions for an epidemic are in place. Depending on the travel patterns of infected humans or infected mosquitos, the epidemic spreads from village to village and into cities.

Figure 3: Example of transmission patterns for yellow fever in East Africa



Strategies for yellow fever control and prevention

Strategy 1. Detect and control outbreaks of yellow fever

An outbreak of yellow fever is defined as at least one confirmed case. Detection and control of a yellow fever outbreak requires a reliable disease surveillance system that will lead to:

- Early detection and immediate reporting of the suspected case of yellow fever.
- Prompt collection of laboratory specimens for laboratory confirmation of a suspected case.
- Advance preparation for implementing emergency immunization activities when an outbreak is confirmed.

An emergency immunization response targets all persons in the area around the outbreak, regardless of their yellow fever immunization history.¹ Advance preparation includes assessing the current availability of vaccines, cold chain supplies, immunization equipment and trained personnel. Emergency immunization activities will require a demand for additional amounts of vaccine and other supplies. Coordination between international, national and local resources that will support the emergency immunization activity should be specified in advance.

Strategy 2. Include yellow fever vaccine in routine childhood immunization schedules

When yellow fever is given only in response to an outbreak, very young children and anyone born after the last outbreak and last yellow fever immunization campaign are left at risk for the disease. They will not be protected against yellow fever because yellow fever vaccine is not part of routine immunization activities for these groups. Consequently, in an outbreak, the incidence rate for yellow fever cases will be higher in children.

To increase protection against yellow fever, integrate the yellow fever vaccine (17D strain) into the national immunization programme's childhood immunization schedule. It is safe and convenient to give the yellow fever immunization to all infants when they come for their measles immunization, usually for infants at least nine months of age. The 17D vaccine should never be given to infants less than six months of age because the risk of extreme complications is high in this age group.

If it is agreed upon and appropriate, begin routine yellow fever immunization of infants with a mass immunization campaign that targets all age groups. Prioritize geographic areas for a mass campaign according to the:

- Interval since the last outbreak;
- Frequency of epidemics in an area;
- Ratio of urban to rural cases:

¹ Planning and conducting emergency yellow fever immunization sessions is described in Section 5.

-
- Vector density;
 - Location of mosquito habitats and infestation;
 - History of previous yellow fever immunization programmes— for example, if coverage is less than 60%, this is not high enough to protect a population from a yellow fever outbreak;
 - Extent of yellow fever surveillance activities and whether the system is detecting cases.

If it is national policy that vaccinated persons must have a card, plan to distribute yellow fever immunization cards during the activity.

Plan the mass campaign during the most optimal season, for example, before the rainy season begins. Define the scope of the mass campaign and the target age groups that will be immunized.

Follow up the mass immunization campaign with focused immunization activities to deliver yellow fever vaccine to immigrants, migrant workers, refugees, and other groups that may have not been included in the mass campaign.

Give infants and young children the yellow fever vaccine as part of the routine childhood immunization schedule.

Routinely monitor yellow fever coverage in the district to identify areas of poor programme performance and focus improvements in these areas.

The tables on the next two pages summarize the role of each level of the health system in strategies for control and prevention of yellow fever.

Table 1: Role of each level of health system in yellow fever surveillance and laboratory support

	Detect and confirm suspected cases of yellow fever	Respond to a confirmed case
Health facility	<p>Use a standard case definition to identify suspected cases of yellow fever.</p> <p>Report them immediately to the next level.</p> <p>Investigate suspected case and complete first two sections of the case investigation form.</p> <p>Take diagnostic samples (serum or liver) and send to designated laboratory to confirm diagnosis.</p>	<p>As soon as yellow fever is confirmed:</p> <ul style="list-style-type: none"> • Conduct an immunization activity. • Start with infants at least nine months of age, and then immunize neighbouring areas. • Work with district level to determine the extent of epidemic (for example, conduct case-based surveillance and mapping). • Report case information to the next level.
District level	<p>Assist health facility staff with case investigation and with collection and transportation of laboratory samples for diagnostic testing.</p> <p>Identify and report trends of increased numbers of cases with “fever of unknown origin” or “fever with jaundice”.</p> <p>Notify national level about suspected case; alert other health facilities.</p> <p>Receive and report laboratory results to the health facility.</p>	<p>According to direction from the epidemic control committee, help health facility to:</p> <ul style="list-style-type: none"> • Conduct an emergency immunization activity. • Conduct an active search for other suspected cases near confirmed case(s); map suspected cases • Collect specimens from any new suspected cases for laboratory confirmation and report to national or district level. <p>Plan case response activities with national level.</p>
Laboratory	<p>Give specimen collection kits, if necessary, to district level or health facility with instructions on specimens to collect, how to collect them, where to send them.</p> <p>Process specimens.</p> <p>Provide results to the reporting health facility and to national level or district medical officer on second part of case investigation form.</p>	<p>Process specimens.</p> <p>Report results promptly to health facility and to national and/or district level.</p>
National programme	<p>Provide a standard case definition for use at all levels. Train and supervise staff in case investigation and specimen collection.</p> <p>Give feedback to reporting levels about confirmed cases. Provide laboratory results to district and/or provincial levels. Make decisions about response to confirmed outbreaks.</p> <p>Collect and analyse routine data to predict or detect possible outbreaks.</p> <p>Develop and integrate plans for emergency immunization response into emergency response plans.</p>	<p>Report outbreak to international health agencies as required.</p> <p>Support epidemic control committee response activities (e.g., case finding, mapping, obtaining supplies and transporting vaccines, and mosquito control) Give feedback on outbreak to reporting levels.</p> <p>Integrate plans for yellow fever outbreak response into emergency response plan.</p> <p>Discuss outbreak response and coordinate preparedness with community leaders and health staff from other levels.</p>

Table 2: Role of each level of health system in prevention of yellow fever

	Routine Immunization with Yellow Fever Vaccine	Mass Campaigns
Health Facility	<p>Include 17D yellow fever vaccine as part of routine EPI childhood immunization schedule (recommend giving at the time infant comes for measles vaccine at age nine months).</p> <p>Use safe injection practices.</p>	<p>Conduct surveillance for priority diseases as a routine activity.</p> <p>Include yellow fever vaccine in routine immunization activities.</p> <p>Conduct health education about yellow fever prevention (e.g., provide information about reducing mosquito burden in or near household).</p>
District Level	<p>Support activities to include yellow fever vaccine in the routine EPI childhood immunization schedule.</p> <p>Ensure safe injection practices, and a reliable supply of vaccine and immunization equipment.</p> <p>Monitor immunization activities.</p>	<p>Monitor and supervise routine disease surveillance; ensure health facilities report as required; provide guidance, support, training when improvement is needed.</p> <p>Collect and analyse routine district-wide data and send to next level (specify the minimum data to be collected from health facilities).</p> <p>Support health facility vector control activities and community education about prevention of yellow fever.</p>
Laboratory		<p>Establish and maintain clear communication methods with each level giving information about the specimens to provide and how to collect and ship them.</p> <p>Ensure health facilities have adequate and appropriate supplies for sending samples (e.g., vials, biopsy needles, case investigation forms).</p> <p>Report positive laboratory results promptly.</p>
National Programme	<p>Review routine EPI programme for feasibility of including yellow fever vaccine in the infant and childhood schedule, if it is not already included.</p> <p>Collect and analyse immunization monitoring data.</p> <p>Use analysis conclusions to take action for improving routine yellow fever immunization services.</p> <p>Provide feedback and support to all levels.</p> <p>Set targets for programme activities and monitor them.</p>	<p>In areas of high risk for yellow fever, initiate and guide planning of mass immunization campaign for all ages.</p> <p>Monitor and supervise staff who collect data to ensure timely routine disease reporting, including zero reporting.</p> <p>Plan and do training for health workers in how to suspect and report yellow fever cases.</p> <p>Give feedback to peripheral levels any time data may indicate conditions favor a possible outbreak.</p>

2. Prepare to conduct district level activities for yellow fever surveillance

Disease surveillance is a key part of communicable disease control. Certain diseases that result in a significant number of deaths and illness are identified as priority diseases for surveillance because action can be taken to limit transmission of the disease. Yellow fever is a priority disease for surveillance because taking specific public health action can control an outbreak and prevent additional cases from occurring.

General tasks in disease surveillance:

- 1) **Detection:** The first opportunity for reporting a priority disease is when a health worker sees a patient and identifies a suspected case of the priority disease.
- 2) **Reporting:** Suspected cases of priority disease are reported to the district level. If yellow fever is suspected, the case is reported immediately.
- 3) **Analysis:** Constant analysis of the routine data is a tool for prompt detection of suspected outbreaks of priority diseases. Health facilities and the district level should review routine data to identify cases that match a case definition of a suspected case of a priority disease and any changes in disease trends that may signal an outbreak.
- 4) **Investigation/Confirmation:** As soon as a case is reported, the health facility and district level begin an investigation to identify the possible causes for disease transmission. The district and national level cooperate in obtaining a diagnostic confirmation of the case.
- 5) **Feedback:** Both the national and district levels provide feedback to other health facilities about progress with control and prevention activities.

2.1 Review the district level tasks for yellow fever surveillance

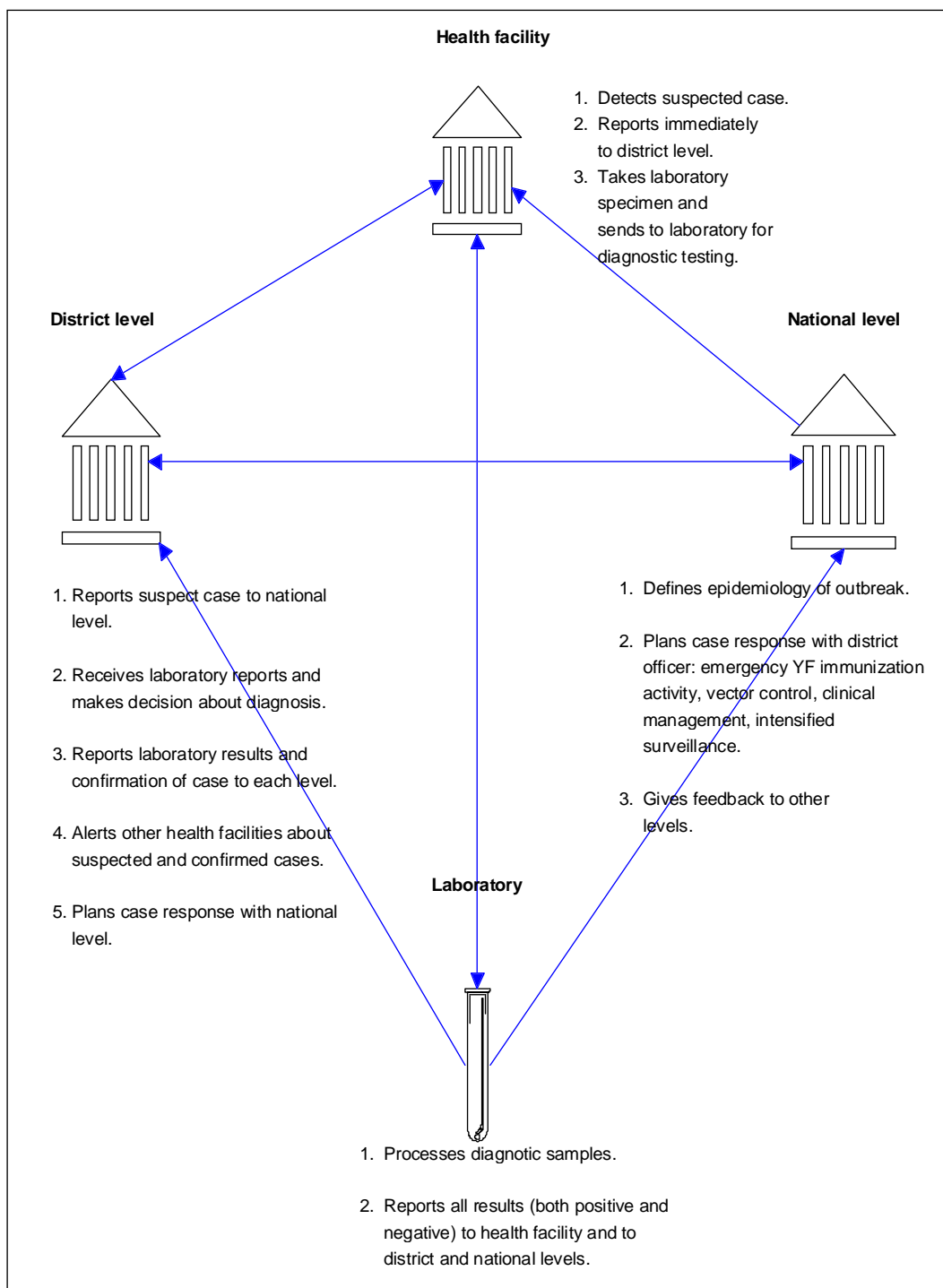
All levels of the health system are involved in surveillance of yellow fever. The role of the district level is to apply national policy recommendations in the district and:

- Make sure that personnel at health facilities in the district know how to identify suspected cases of yellow fever.
- Make sure that health facilities use a standard case definition to report suspected cases of yellow fever.
- Assist health facilities with investigation of suspected cases.

-
- Collect samples for diagnostic testing and laboratory confirmation. If necessary, transport samples to a drop-off point or specified laboratory.
 - Notify the national level about the suspected case. Alert other health facilities in nearby areas about the potential for additional cases.
 - Receive and report laboratory results about confirmed cases.
 - Coordinate the response to the confirmed case with a district emergency response committee.
 - Carry out intensified surveillance activities to identify additional cases in areas where the patient lived, worked or travelled. Collect diagnostic specimens from any new suspected cases.
 - Monitor and supervise routine disease surveillance activities. Analyse data for trends suggesting a yellow fever outbreak. Report data from routine activities to the national level on time.
 - Assist and support health facilities with the integration of yellow fever vaccine into the routine childhood immunization schedule. Make sure vaccine and immunization supplies are available for routine yellow fever activities.

The diagram on the next page describes the relationship between each level in the health system which has activities for yellow fever surveillance.

Figure 4: Yellow fever surveillance system



2.2 Identify reporting sites in the district

Review the list of health facilities in the district including community-based health services and reporting sites.

- 1) Make sure that all reporting sites within the district are included in the list.
- 2) Verify the following information for each reporting site:
 - The name and address or locating information for each health facility.
 - The name of the health facility staff person who is responsible for yellow fever surveillance at the health facility.
Note: If a specific person on the health facility staff has not been identified to report information about priority diseases seen at the health facility, assist the health facility in identifying who will be responsible for disease reporting from the health facility.
 - Method for contacting health facilities (telephone number, facsimile number, or other method for communicating between the health facility and the district level).
- 3) Record the information on a reference form such as the example below. Periodically, review the list to make sure it is complete and up to date.

Sample list for district reporting sites and contact information

Name of health facility	Address or location of health facility	Person responsible for yellow fever surveillance	Telephone or facsimile number (or other contact information, e.g. e-mail)
Lima Health Centre	Box 123 Mlima zone	Dr. Moyo	Tel: 123-458 or send message by railroad's daily radio contact with Mlima station.
Nyota Primary Health Care Centre	Box 14, Road 5A Nyota Village	M. Kiyondo	Tel: 456-123 facsimile: 456-129
St. Lucy's Mission Hospital	Box 21 Bandari Port	Sister Kira	Tel: 455-234 or send message in daily radio contact with district mission hospital.

2.3 Review procedures for reporting yellow fever

Review the standard procedures for disease reporting in the district to make sure they include activities for reporting cases of yellow fever. Confirm that health facility staff know how to:

- 1) Use a standard case definition to identify suspected cases. The standard case definition should be used throughout all levels of the reporting system — from the peripheral level (health facilities and other points where patients have contact with the health system) to the national level. WHO recommends the following case definition for yellow fever:

WHO case definition for yellow fever surveillance:

Suspected case:	An illness characterized by an acute onset of fever followed by jaundice within two weeks of onset of the first symptoms AND one of the following: bleeding from the nose, gums, skin, or gastrointestinal tract OR death within three weeks of the onset of illness.
Confirmed case:	A suspected case that is confirmed by laboratory results or linked to another confirmed case or outbreak.
Outbreak:	An outbreak of yellow fever is at least one confirmed case.

- 2) Follow district procedures for reporting suspected cases of yellow fever immediately—as soon as a suspected case is identified. Refer to the steps for reporting suspected cases in Section 3.2.
- 3) Report “zero cases” when no yellow fever cases were suspected or confirmed during the reporting period.

If procedures for reporting suspected cases of yellow fever are not specified or are not known in the district, make improvements as needed. For example, meet with health facility supervisory staff to define the reporting procedures and communicate them to the health facility staff.

2.4 Review availability of supplies for collecting and transporting specimens

It is not possible to conduct the diagnostic tests for yellow fever at every health facility. Specimens collected at the location of the suspected case are sent to a qualified national yellow fever reference laboratory or WHO Collaborating Centre for analysis.

Before an outbreak occurs:

- Determine the availability of appropriate laboratory supplies for specimen collection and transport at each health facility, especially in geographic areas where yellow fever cases have occurred in the past.

Find out if a set of supplies can be set aside for use when yellow fever is suspected. The checklist on the next page can be used to assess the availability of recommended supplies at each health facility.

- Assemble and keep at the district level a minimum set of supplies for collecting specimens in the event a health facility does not have the required supplies during an urgent situation.

Note: Contact the national coordinator for yellow fever surveillance, if one has been selected, to coordinate preparedness activities for collecting diagnostic samples.

Checklist of supplies for laboratory confirmation of yellow fever

For taking blood samples:	
_____	Sterile vacutainer (blood collection device) or sterile needle and sterile syringe
_____	Sterile ordinary test tube, if a sterile syringe is used
If the health facility has a centrifuge:	
_____	A supply of sterile centrifuge tubes
_____	Sterile pipette
_____	Sterile glass or plastic tube, or a bottle with a screw-on top
For storage of specimens before shipment:	
_____	Access to a freezer or cold box that can freeze at temperatures -20°C or below, or a standard refrigerator
For packing and shipping blood samples:	
_____	A cold box with frozen icepacks or a vacuum flask or cardboard box lined with two to three inches of polystyrene or foam rubber and cotton wool for cushioning the sample and avoiding breakage
_____	Shipping labels for addressing shipment to reference laboratory
_____	Labels for marking "biological materials" on the outside of the shipment box
_____	Labels for marking "store in a refrigerator" on the outside of the shipment box
_____	A supply of case investigation forms
For collecting liver samples:	
_____	A liver biopsy needle
_____	A vial containing 10% formalin in normal saline or Ringer's lactate solution
(Note: In some countries, kits for collecting liver samples from fatal cases are available from the national yellow fever or viral haemorrhagic surveillance programme. Find out from the national programme how would one be requested.)	

2.5 Review procedures for safe packaging and transport of specimens.

- 1) Detailed instructions for packing and shipping infectious substances are in Section 4.2 and in Annex 8. Review the instructions and decide if the appropriate packing materials are available. If not, obtain a supply to set aside for use in an urgent situation.

Reference laboratory for confirming yellow fever

WHO Collaborating Centre: _____
Contact person: _____
Telephone: _____
<i>or</i>
National laboratory: _____
Contact person: _____
Telephone: _____

- 2) If you do not know the designated reference laboratory that will receive specimens from this district, ask the national level to identify the designated reference laboratory.² Record this on the form for future reference during an urgent situation how to contact the laboratory.
- 3) Ask the national coordinator about procedures for forwarding the specimen either to the national level or directly to the reference laboratory. In some cases, the district level may need to transport the specimen to the national level or to a designated airport.
- 4) Be prepared to assist the health facility with transportation of the specimen. For example, the district level may need to provide road transportation to the health facility to collect the specimen and then return to a pick-up point for forwarding the specimen to the national level or reference laboratory. Determine alternate routes to and from the health facility in the event usual routes are unpassable.
- 5) If airline or commercial road transportation services will be used, identify the contact persons. Meet with them to explain the importance of the activity. Discuss the special packaging that will be used and give reassurance that the shipment will be prepared safely. Find out the schedules and other requirements for shipping the specimen. Record the information for use in an urgent situation. Instructions for packaging infectious material for air shipment are in Annex 8.

² A list of WHO Collaborating Centers with laboratory facilities for confirming yellow fever is in Annex 4.

2.6 Review procedures for monitoring yellow fever surveillance activities

Assess monitoring practices in the district to make sure they are taking place as recommended by national policy. Determine whether monitoring results are used to measure the impact of immunization and surveillance activities for yellow fever. Take action to improve activities as soon as problems are identified.

1) Make sure procedures are in place for collecting information about:

- Yellow fever immunization coverage at each health facility and in the district.

Note:

The **denominator** for calculating yellow fever immunization coverage is the size of the population targeted for yellow fever immunization activities in the district or health facility catchment area.

The **numerator** is the number of people who actually received a dose of the vaccine.

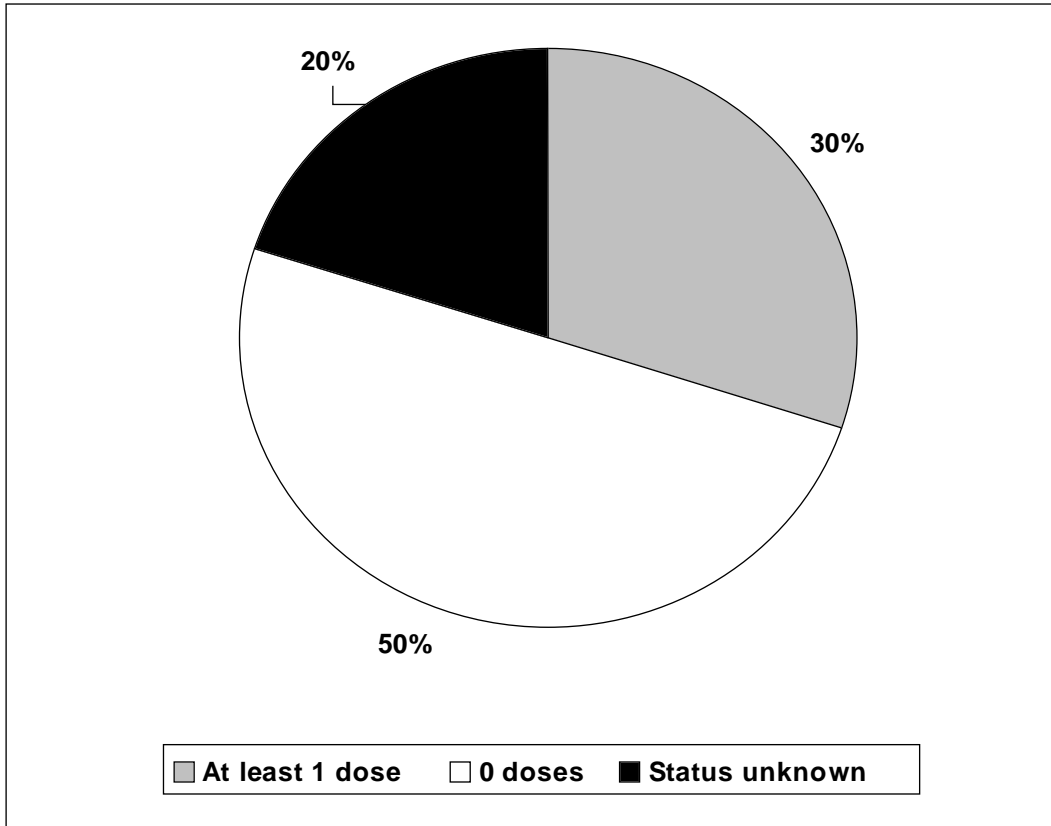
For example, if yellow fever is included in the routine childhood EPI schedule, collect information from each health facility catchment area about the number of infants who received a dose of yellow fever vaccine during the reporting period.

- Number of suspected cases that had laboratory results for diagnostic testing.
- Number of confirmed cases at each health facility.
- Location of suspected and confirmed cases in each health facility's catchment area.
- Interval between the time that the first suspected case is identified and when an actual response to the case occurs.

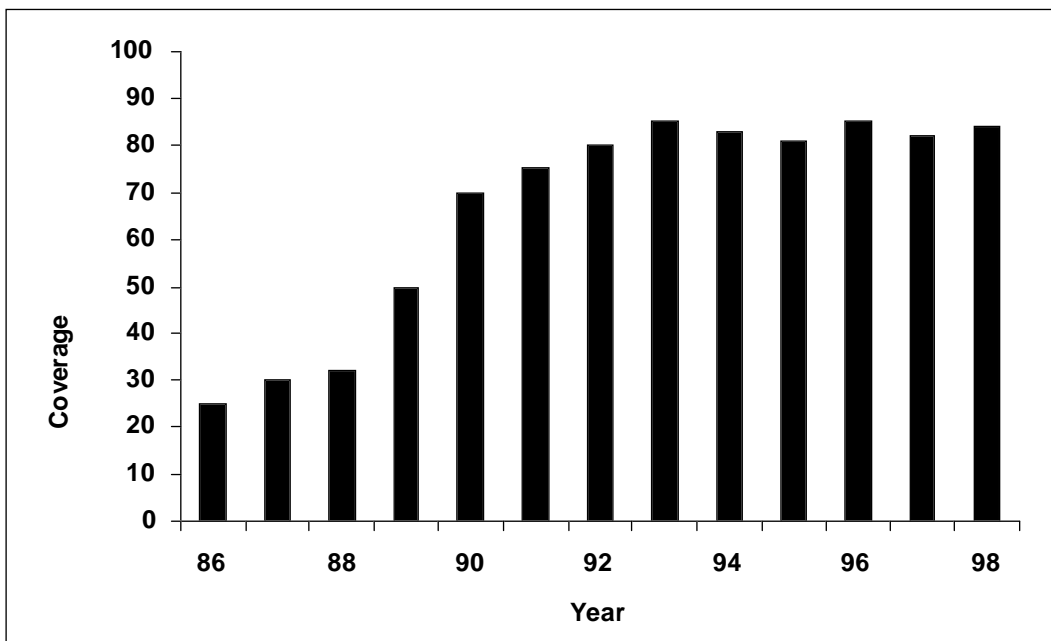
2) Make sure that monitoring results are recorded and analysed.³ Determine whether analysis results are presented in a clear graphic format, such as graphs, tables, charts or spot maps (see samples below).

³ A sample line listing form for recording information from case investigations of suspected cases of yellow fever is attached as Annex 7.

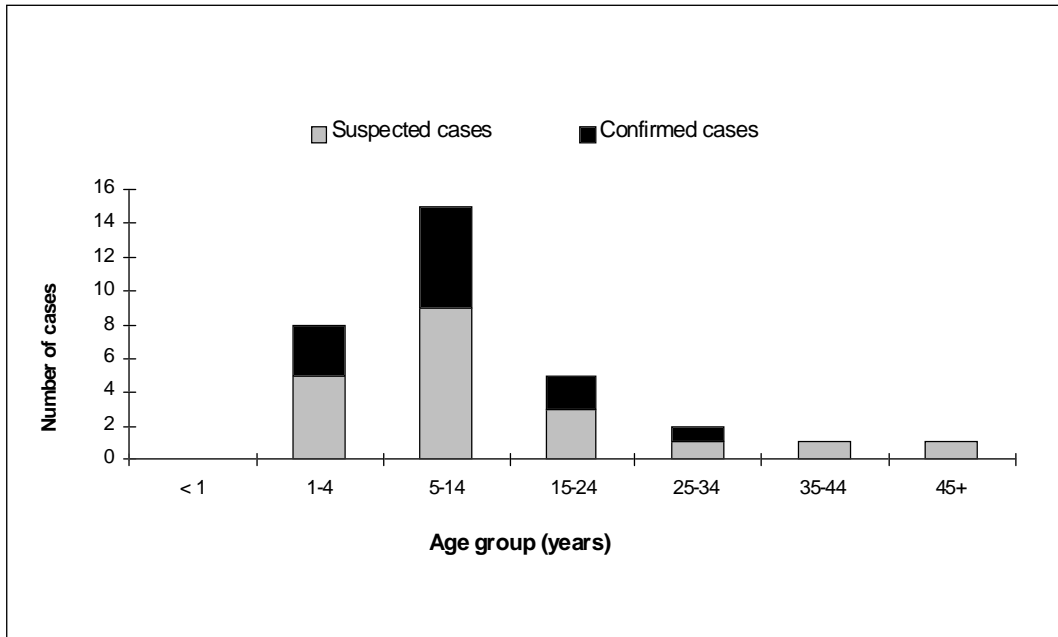
Sample 1— Pie chart: Immunization status of 30 confirmed yellow fever, District “X”



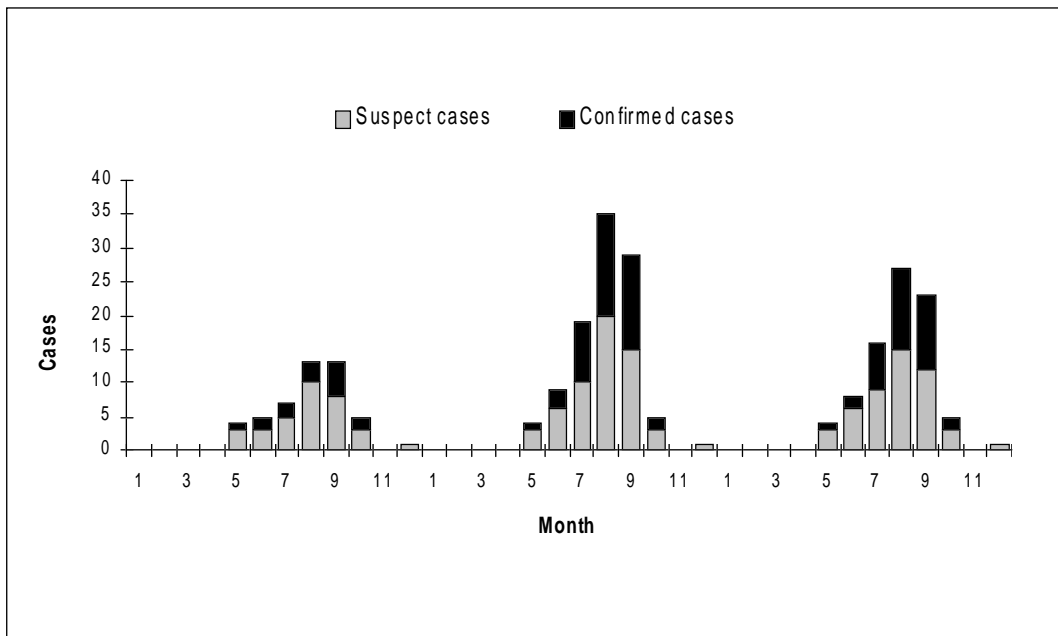
Sample 2— Bar chart: Routine immunization coverage of infants, Districts “X”, 1986-1998



Sample 3 — Bar chart: Age group of suspected and confirmed cases, District “X”, 1998



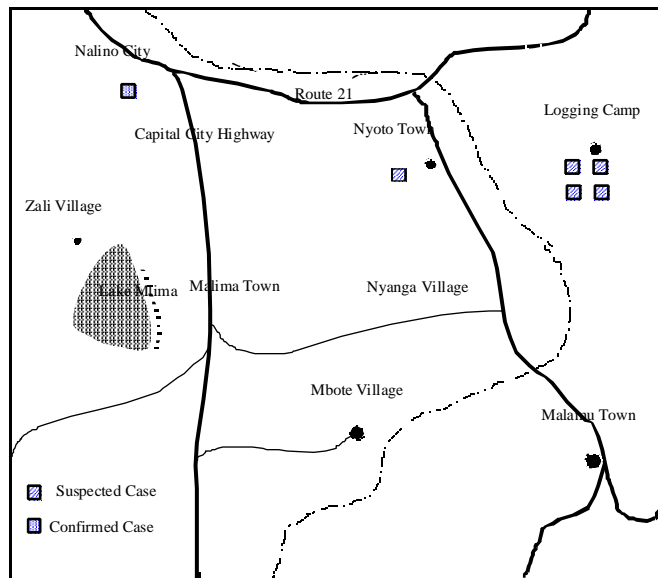
Sample 4— Bar chart: Suspected and confirmed cases by month, District “X”, 1996-1998



Sample 5 — Table, showing immunization coverage results and targeted age groups for yellow fever immunization campaigns in the district

Month	Year	District	Age group targeted	Number targeted	Number reached	% reached
May	1991	X	9 months to 30 years	30 000	25 000	83
June	1997	X	9 to 59 months	5000	4000	80

Sample 6 — Spot map of a sample district map showing the location of previously confirmed and suspected yellow fever outbreaks.



Use a spot map to identify areas of potential risk for yellow fever outbreaks. To compile a spot map, plot the following information on a map of the district:

- location of the health facilities and their catchment areas;
- geographic areas such as forests, savannah areas, villages, settlements and cities;
- location of suspected and confirmed cases;
- location of any previously confirmed yellow fever cases; indicate whether the case originated in a forested area, a village, or a city;
- work sites such as logging or mining camps with transient workers and known sites for herding or farming activities located near yellow fever endemic zones.

For sample 7 — Line-listing, see Annex 7.

2.7 Identify an emergency response committee in advance

When a case is confirmed, response activities will be planned in a district emergency response committee. It can save time during an outbreak if key members of the response committee are identified in advance. Refer to Section 5 for details about the role of the emergency response committee in a yellow fever outbreak.

Section 2 describes the steps for preparing to respond to reports of yellow fever.

Sections 3, 4, and 5 describe what to do once a suspected case is detected and reported.

Section 5 describes the activities for responding to a confirmed outbreak, including the role of an emergency.

3. Detect yellow fever

A case of yellow fever is detected when it is identified and reported.

3.1 Identify suspected cases

In an outbreak of yellow fever, identification of a suspected case is based on the signs and symptoms seen in the current outbreak. In a *non-outbreak situation*, identifying a suspected case of yellow fever is more difficult. The early signs of yellow fever — fever, headache, nausea and vomiting — are also signs of other fever-producing diseases commonly seen in the health facility. A health worker might not suspect yellow fever until treatment for other illnesses is not successful, or if the patient’s condition worsens and additional signs develop.

Stage of yellow fever	Common signs	Differential diagnosis
Early signs or signs in mild cases of yellow fever (three to six days after bite from infected mosquito)	Fever Headache Nausea Vomiting	Malaria Influenza Dengue fever (Non-haemorrhagic)
Classic signs of yellow fever (four to ten days after onset)	Sudden onset of fever Headache Nausea Vomiting Chills Back pain Generalized muscle pain Red eyes (conjunctival injection) Dark urine Jaundice (although jaundice may be absent in some cases)	Malaria Typhoid fever Rickettsial infections Other arboviral fevers
Later stages of yellow fever (seven to ten days after onset)	Brief improvement followed by: Jaundice Blood in vomit (“coffee grounds” seen in vomit) Bleeding from the gums, nose, or gastrointestinal tract Blood in urine Decreased / no urine production Shock Slow pulse in relation to fever Death	Other diseases with signs of bleeding and signs of liver and renal dysfunction: Viral hepatitis Severe malaria Other viral haemorrhagic fevers: (Lassa, Marburg, Ebola, Crimean-Congo, Hantaan) Leptospirosis Surgical or toxic causes of jaundice

Health workers in yellow fever transmission zones should be aware of the signs and symptoms of yellow fever seen in previous cases in their geographic area. Because the clinical presentation of yellow fever can vary from mild to more serious signs of illness, detection of the suspected case may not occur until yellow fever is suspected for a hospitalized patient who is seriously ill. Once the suspected case is identified, immediately take steps to confirm and respond to the case.

3.2 Receive reports of suspected cases from the health facility

When a health facility reports a suspected case, make sure to collect at least the following information:

- The patient's name, locating information, and patient record number.
- The patient's symptoms: did the patient have fever and jaundice or any signs of bleeding (hemorrhage) or reduced production of urine.
- The date of onset for any of the symptoms that developed.
- The name of any districts or areas where the patient lived or visited in last two weeks.
- The presence of other cases of fever and jaundice in the patient's household or in districts where the patient lived or visited in last two weeks?
- The patient's yellow fever immunization history: did the patient ever receive at least one dose of yellow fever vaccine?

Health facilities can use the top part of a case investigation form to record the information for reporting to the district level. Please see the example of the top part of the case investigation form on the next page.

Case investigation form : Suspected yellow fever

As soon as Yellow fever is suspected, contact :										
District communicable disease manager:			Telephone number: _____			Facsimile number: _____				
OR District EPI programme manager:			Telephone number: _____			Facsimile number: _____				
1. Record general information about the patient:					Date of report:					
Patient's name and patient record number:					Sex: M [] F []					
Address:					Patient's occupation:					
District: State or Province:					Village or municipality:					
Patient's date of birth					Patient's age (if date of birth unknown):					
dd			mm			yy				
2. Does suspected case have:				Date of onset			3. Record travel and yellow fever immunization history.			
Fever (>38°C or >101°F) That did not respond to antimalarial treatment	Y	N	U	dd	mm	yy	List names of other areas or districts that patient visited during the last two weeks:			
Jaundice	Y	N	U	dd	mm	yy				
Slow pulse in relation to fever	Y	N	U	dd	mm	yy	Have cases of fever and jaundice been seen or reported in areas or districts that patient visited during the last two weeks?	Y	N	U
Bleeding from the nose, gums or skin or gastrointestinal tract	Y	N	U	dd	mm	yy				
Reduced amount of urine	Y	N	U	dd	mm	yy	Has the patient ever received at least one dose of yellow fever vaccine?	Y	N	U
Elevated level of protein in urine	Y	N	U	dd	mm	yy	What was final outcome for patient? (<i>circle one</i>) Leaving Dead Unknown If patient died, record date of death: (dd) _____ (mm) _____ (yy) _____			
Reported by: _____					Contact number for health facility: _____					

3.3 Report suspected cases to the national authorities and the reference laboratory

Immediately contact the appropriate national level programme manager according to national policy. For example, contact the EPI programme manager, the communicable disease programme manager, or the yellow fever laboratory or national yellow fever coordinator, if one has been selected.

- 1) Request guidance and assistance for collecting the appropriate specimens for laboratory confirmation of the case. Request any support that will be needed to collect or transport the samples.
- 2) Use the information from the health facility's report to begin investigating the case. How to investigate a suspected case is described in Section 4 of these guidelines.
- 3) Advise the health facility to:
 - Use appropriate barrier nursing methods with the suspected case until yellow fever is confirmed.
 - Take steps to reduce mosquito breeding sites around the hospital and near the patient's home. For example, empty uncovered water receptacles. Clean and refill them. Cover them with a lid. Remove other items that collect water such as bottles or discarded tyres.
 - In an epidemic, when more than one or two suspected cases have presented in the health facility, place patients with suspected cases of yellow fever in a room with screened windows or use a bed net to prevent mosquitos from biting the infected patient. (Patients who are in the later stages of the illness, after jaundice has appeared, are not infectious for mosquitos) Additional guidance for clinical management of yellow fever is described in Section 5.1.
- 4) Assist the health facility in the identification of any additional cases.

Note:

- a) During the analysis of routine reporting, identify any gaps in the reporting of suspected cases. For example, make sure that the number of reported suspected cases matches the number of reporting forms (or case investigation forms) and the number of collected blood samples. If cases are being reported, but no action is being taken to investigate them, find out what has caused the problem and make improvements.
- b) Investigate suspected cases or outbreaks identified during routine reporting and report them to the national level.

4. Confirm yellow fever

Yellow fever is confirmed if laboratory results show:

- Isolation of the yellow fever virus, or
- Presence of yellow fever specific IgM, or
- A four-fold or greater rise in serum IgG levels between the acute and convalescent serum samples, or
- Positive post-mortem liver histopathology, or
- Detection of yellow fever antigen in tissues by immunohistochemistry, or
- Detection of yellow fever virus RNA genomic sequences in blood or tissues.

Note:

Make sure health staff who investigate suspected cases and handle infectious blood are immunized against yellow fever. Health staff should use appropriate barrier nursing practices if contact with blood and other infectious body fluids is likely.

4.1 Investigate the suspected case

Use a standard yellow fever case investigation form to guide the investigation of the suspected case. A sample case investigation form is on the next page. There are two parts to the form. Record information about the patient and the patient's history in the top half of the form. Record the laboratory results and the final classification of the case in the second half of the form.

Results of the investigation will provide:

- General information about the patient (for example, locating information, age and occupation).
- The patient's symptoms and their date of onset.
- Any recent travel the patient may have taken to areas where yellow fever is endemic or where cases of fever and jaundice have been reported.

-
- The patient's immunization history noting whether the patient has ever received at least one dose of yellow fever vaccine.
 - Results of laboratory analyses of blood or tissue specimens.

Obtain information from the patient and from available records at the health facility. If the patient is too ill to answer, or has died, ask family members in the patient's household to provide information about the patient's symptoms, travel, and immunization history.

Case investigation form : suspected yellow fever

As soon as Yellow fever is suspected, contact :										
District communicable disease manager:					Telephone number: _____ Facsimile number: _____					
OR District EPI programme manager:					Telephone number: _____ Facsimile number: _____					
1. Record general information about the patient:					Date of report:					
Patient's name and patient record number:					Sex: M [] F []					
Address:					Patient's occupation:					
District: State or Province:					Village or municipality:					
Patient's date of birth					Name of head of patient's household or village chief:					
dd	mm	yy	Patient's age (if date of birth unknown):							
2. Does suspected case have:				Date of onset			3. Record travel and yellow fever immunization history.			
Fever (>38°C or >101°F) That did not respond to antimalarial treatment	Y	N	U	dd	mm	yy	List names of other areas or districts that patient visited during the last two weeks:			
Jaundice	Y	N	U	dd	mm	yy				
Slow pulse in relation to fever	Y	N	U	dd	mm	yy	Have cases of fever and jaundice been seen or reported in areas or districts that patient visited during the last two weeks?	Y	N	U
Bleeding from the nose, gums or skin or gastrointestinal tract	Y	N	U	dd	mm	yy				
Reduced amount of urine	Y	N	U	dd	mm	yy	Has the patient ever received at least one dose of yellow fever vaccine?	Y	N	U
Elevated level of protein in urine	Y	N	U	dd	mm	yy	What was final outcome for patient? (<i>circle one</i>) Living Dead Unknown If patient died, record date of death: (dd) ____ (mm) ____ (yy) ____			
Reported by: _____					Contact number for health facility: _____					

Laboratory transmittal and final classification of the case

Specimens collected (Circle one)	Date specimens collected (dd/mm/yy)	Date received in laboratory (dd/mm/yy)	Type of test	Results				Date results sent to MOH (dd/mm/yy)	Date results received at MOH (dd/mm/yy)
				Pos	Neg	Not processed	Unk		
Blood			IgM						
			IgG (acute)						
			IgG (convalescent)						
Malaria slide			Microscopy						
Other									
1. Were specimens or isolates sent to another laboratory? (<i>circle one</i>) Yes No Unknown				2. If YES, record laboratory's name, address, and telephone number:					
3. What is the final classification of the case? (<i>circle one</i>) Suspected Confirmed Discarded Unknown									
4. If case discarded as yellow fever, record diagnosis:				5. What was final outcome for patient? (<i>circle one</i>) Living Dead Unknown					
				6. If patient died, record date of death: (dd) ____ (mm) ____ (yy) ____					
Investigator's name: (<i>please print</i>)				Signature:					
Address:				Telephone number:					

4.1.1 Collect general information about the patient

Collect and record in the top half of the case investigation form:

- The date the district level was first notified about the case.
- The patient's name and clinic identification number.
- The patient's address, sex, occupation, date of birth or approximate age (if the date of birth is not known).
- The head of the patient's household and the name of the village chief.
- The name of the health facility where the patient was treated.

4.1.2 Record the patient's history

- 1) Collect and record on the form whether any of the following signs are present:
 - Fever higher than 38°C (101°F)
 - Jaundice
 - Slow pulse in relation to fever
 - Bleeding from the nose, mouth, skin or gastrointestinal tract
 - Other signs suggesting yellow fever (for example, reduced production of urine or an elevated level of protein in the urine).
- 2) For each symptom, record the date of onset. If the patient did not survive, record the date of death.
- 3) List names of areas or districts that the patient has visited or lived in during the last two weeks.
- 4) Find out if any cases of fever and jaundice have been reported from the areas where the patient has lived or travelled during the last two weeks.
- 5) Record whether the patient's immunization history includes at least one dose of yellow fever vaccine given at any time in the past.

The second half of the case investigation form is used as a laboratory transmittal form to accompany the diagnostic samples and for recording the final classification of the case.

4.2 Collect and transport laboratory specimens for diagnostic testing

Usually the laboratory will request two blood samples. In the event the case is deceased, the laboratory will request at least a tissue sample, usually a liver sample.

Note:

Treat blood and tissue samples from the suspected yellow fever patient as infectious material. Transmission of dangerous diseases can occur through accidental needle injuries and other accidental contact with infectious body fluids. Use all relevant safety precautions when handling blood. If possible, wear at least one pair of gloves.

4.2.1 Contact the reference laboratory

If the national level or the reference laboratory has not yet been contacted, contact them now. They will provide specific guidance about collecting and sending diagnostic samples to the reference laboratory.

4.2.2 Collect two blood samples

Assist the health facility in collecting and packaging the blood samples.

- 1) Refer to the checklist in Section 2.4 that describes the required supplies for collecting blood or tissue specimens.
- 2) Collect one blood sample as soon as the patient is admitted to hospital or suspected as having yellow fever. This is the acute sample. Send it immediately to the laboratory.
- 3) If a syringe is used, transfer the sample to a sterile plain centrifuge tube, sterile ordinary tube, or vacutainer tube.
- 4) Immediately label the tube or vacutainer with the patient's name, date of birth, and sex. Include the name of the health facility and the date the specimen was collected. Make sure the information on the label matches the information on the case investigation form.
- 5) Let the sample stand at room temperature for a half to one hour.
- 6) Spin the sample in an ordinary or refrigerated centrifuge to obtain the serum. Spin at 1500 to 2000 revolutions per minute for 15 to 20 minutes.

If a centrifuge is not available, allow the sample to stand at room temperature until clot retraction has occurred. Remove the serum from above the clot.

- 7) Use a sterile pipette to transfer the serum to a plain sterile tube or bottle with a screw top. The tube or bottle can be glass or plastic. Use a marker that will not wash off to record the identifying information on the sterile tube or bottle. Alternatively, write the information on an adhesive tape label using an indelible ink marker or pencil. Make sure the identifying information matches the information on the case investigation form.
- 8) Make sure that the screw tops on the bottle are tight. Secure the screw caps with adhesive tape.

-
- 9) If samples are being transported to the laboratory within a few hours, **refrigerate but do not freeze them.**
If the samples must be stored for more than 24 hours, freeze them at -20°C or colder. If this is not possible, store them in the refrigerator.
 - 10) Use a cooler or ordinary domestic vacuum flask to transport the samples. Make sure to pack the samples with cotton wool against the walls of the cooler to avoid breakage especially if glass tubes or bottles are used.
If no flask is available, make a cooler from a cardboard box lined with two to three inches of polystyrene or foam rubber and with cotton wool. Place tubes or bottles in a plastic bag, if one is available, and surround it with packing material to avoid breakage.
 - 11) Seven to ten days later (or, at the time a hospitalized patient is discharged), collect a second blood sample and send it to the laboratory. If the patient dies, collect a post mortem blood sample. This is the **convalescent sample.**

4.2.3 Collect a liver sample to confirm a fatal case

Specific instructions for collecting a liver sample from a fatal case are available from the national level or the reference laboratory. They may provide you with a kit that contains supplies and instructions for taking a liver sample and sending it to a reference laboratory.

- 1) Use a liver biopsy needle or biopsy punch to take a sample of liver tissue. This is especially important if a blood sample was not collected.
- 2) Place the liver sample in a vial containing 10% formalin in normal saline or Ringer's lactate solution.

4.2.4 Prepare a laboratory transmittal form

Use the case investigation form (with the top half completed) as a laboratory transmittal form. Results of the laboratory testing can be recorded on a copy of the form and returned to the health facility and district office for further decisions and actions.

Note:

If possible, prepare a supply of forms that have self-carbons because at least three copies need to accompany the laboratory specimens.

4.2.5 Transport specimens to the reference laboratory

Collect the specimen, if necessary, from the health facility. Deliver it to the pick up point for forwarding to the national level or reference laboratory. Depending on the procedure in your area, the district or national level should contact the reference laboratory to alert them that a specimen is being sent to them. The laboratory may have specific instructions for the shipping address or other administrative requirements.

Detailed instructions for packing and shipping a specimen by commercial air carrier are in Annex 8.

4.3 Report the confirmed case

When the sample is received in the laboratory, the laboratory will record the date they received the sample in the laboratory. Laboratory results will be sent to the district office and the health facility.

Report *all* laboratory *and* investigation results as required to the national level.

- 1) Make sure to record the dates the results were sent from the laboratory and received at the health facility.
- 2) Update the spot map to show the location of suspected and confirmed cases in the area around the health facility. Also make sure the map contains information about yellow fever immunization coverage in the health facility catchment area.
- 3) Keep an accurate line listing of information from the case investigation forms. The line listing should include at least: the patient's name, name and location of the health facility reporting the suspected case, the patient's symptoms and their date of onset, the patient's travel history and immunization status, date the laboratory samples were collected, their results and the date they were sent to the district level, and any follow up actions that were taken.

A sample line listing form is in Annex 7.

5. Respond to a confirmed outbreak

Establish a district yellow fever epidemic control committee to prepare for and coordinate the case response activities. If yellow fever is not frequently seen in the district, a general emergency response committee can assume the responsibility for the response to the outbreak of yellow fever. The epidemic control committee should define the target population at risk for yellow fever and select immediate and long-term responses to the outbreak.

Response actions for a confirmed outbreak of yellow fever

Immediate actions:

- Strengthen clinical management of yellow fever.
- Plan the response activity.
- Implement the plan.
- Identify additional cases through intensified surveillance activities.
- Carry out mosquito control activities.
- Alert nearby areas about the outbreak.

Long-term actions:

- Give priority to the inclusion of yellow fever vaccine in the routine childhood EPI schedule.
- Develop and promote community education interventions for prevention and control of yellow fever.

5.1 Strengthen clinical management of yellow fever

Give advice and support to the health facility about managing the cases of yellow fever present in the health facility. If resources are limited, identify and support a minimum level of recommended case management steps. At a minimum:

- 1) Monitor the patient for fever, dehydration, restlessness, and other infections such as malaria or a bacterial infection.
- 2) Treat the patient's clinical signs with available drugs or therapies.

**Recommended drugs or therapies for treating
yellow fever and concurrent infections**

For fever:	Give paracetamol.
For dehydration:	Give oral rehydration salts.
For restlessness:	Give diazepam.
For malaria:	Give an antimalarial recommended for your area.
For bacterial infections:	Give antibacterials recommended for your area.

5.2 Define the case-response activity

The outbreak response depends upon the extent of the outbreak and a description of the population at risk for yellow fever transmission.

- 1) As soon as possible, meet with the members of the epidemic control committee or emergency response team to coordinate the response to the confirmed outbreak. Include health facility staff in planning and carrying out these activities.

If a district response team was not created in advance, assemble one now. Include at least: a clinician, a public health or vector control officer, the national EPI and communicable disease programme managers, and the national level coordinator for yellow fever, if one has been selected.

- 2) In the committee, review the findings from the investigation of the suspected case. For example, consider the:
 - location of the patient's household and work site, and
 - patient's travel and immunization history.
- 3) Review information about the geographic area around the case and likely areas of potential transmission. For example, be sure to consider the:
 - yellow fever immunization coverage rates in the area around the case
 - possible sources of mosquitos in the area
 - likelihood of potential transmission based on the location of neighbouring villages, transportation routes, and any nearby urban areas with crowded housing areas or poor sanitation.
- 4) Prepare a description of the extent of the outbreak that includes the target population at risk and priority geographic areas for response activities.

5.3 Conduct an emergency immunization activity

Any person who is not immunized against yellow fever is at risk for the disease. In an outbreak situation, the target population for an emergency immunization activity is the general population living or working in the same area as the patient. If initial resources are limited, the primary target population for yellow fever immunization is children of nine months up to 14 years of age.

Start the immunization activity as soon as possible after the outbreak is confirmed. Coordinate plans for the activities with the national level EPI and communicable disease programme managers. Using data from the following activities, estimate costs for conducting the emergency immunization activity.

- 1) Select the immunization sites and schedule them.
 - If the case occurred in a rural area, consider including neighbouring villages in the emergency activity.
 - If the case occurred in an urban area, identify the health facilities that will participate in the activity. Identify any additional sites or hard-to-reach areas. For example, use a mobile site to reach a transient worker's camp that may not be served by a fixed site.
- 2) Estimate the size of the target population.
 - The size of the target population is the size of the general population living or working in the same geographic area as the patient.
 - If the activity will only target children of nine months up to 14 years of age, multiply the size of the general population in the target area times 45% (0.45) to obtain the target population.
- 3) Estimate the amount of required vaccine for the emergency activity. The estimate should include amounts that will be lost to wastage and set aside for provision of a reserve stock.
 - Assume a wastage factor of 1.2%. To estimate the number of doses including wastage, multiply the size of the target population times 1.20 to obtain the total number of doses required.
 - Assume a reserve stock of 25%. To estimate the number of doses including an amount for reserve stock, multiply the estimate of the number of doses of vaccine including an amount for wastage (see the result for calculating wastage in the previous step) times 1.25.
 - 17D yellow fever vaccine is most commonly packaged in vials of 20 doses, although other dose sizes are available and their prices may vary. Divide the total number of estimated doses (see the result for calculating a reserve stock above) by the number of doses in the vial, or 20, if 20-dose vials will be ordered.
 - Calculate the amount of diluent that will be needed to reconstitute the vials of vaccine. The ratio of diluent to yellow fever vaccine is one to one. That is, for each vial of vaccine, request a vial of diluent. Use a diluent recommended by the vaccine manufacturer.
 - Estimate the quantity of syringes, needles, and other immunization supplies.

Note:

Emergency supplies of 17D yellow fever vaccine are likely to be shipped with an adequate supply of single-use auto-destruct needles and syringes (that can only be used one time), and other immunization supplies such as puncture-resistant containers for collecting used needles and syringes.

A request for an emergency supply of vaccine will be filled, based on the size of the target population for the emergency immunization activity. It may not be necessary to provide the donor with a detailed estimate for each item, if the donor bundles supplies of vaccine with the appropriate quantity of auto-destruct needles and syringes.

- 4) Estimate the amount of cold-chain supplies for conducting the emergency activity.
 - Yellow fever vaccine must remain frozen during storage and transportation. Make sure there is enough capacity to store extra amounts of the vaccine during storage and transportation to the immunization site.
 - Contact the national EPI programme manager or, if one has been selected, the national coordinator for yellow fever surveillance, to request additional cold chain supplies (such as icepacks and vaccine carriers) for the emergency immunization activity.

Minimum temperatures for storing yellow fever vaccine

Central store:	Up to six months at -15°C to -20°C .
Regional store:	Up to three months at -15°C to -20°C .
During transport to district:	-20°C to $+8^{\circ}\text{C}$.
At a fixed immunization site:	Up to one month at $+4^{\circ}\text{C}$ to $+8^{\circ}\text{C}$.
With a mobile immunization team:	Up to one week at $+4^{\circ}\text{C}$ to $+8^{\circ}\text{C}$.

- 5) Request the vaccine and immunization supplies.
 - Coordinate the request for vaccine with the national level. If a national reserve stock of yellow fever vaccine is not available, the national EPI programme manager or the national yellow fever coordinator will request an emergency supply from WHO.
 - Provide additional record keeping supplies for the emergency activity (such as tally sheets and immunization cards).

-
- 6) Select vaccinator teams and provide training.
- A rural site may only need one team of vaccinators. A crowded urban site requires more than one team. Select at least two vaccinators and one recorder for each site for every 100 to 150 people expected at the immunization site.
 - A recent study in West Africa estimated that 231 per 100 000 people in the local community suffered from abscesses caused by unsafe injections. Make sure that health workers know and use safe injection practices in any immunization activity.⁴
- 7) Use recommended immunization practices. At a minimum, make sure health workers know how to:
- Reconstitute the yellow fever vaccine correctly.
Vaccine is reconstituted by adding the appropriate quantity of diluent to the freeze-dried vaccine. Reconstitute the vaccine by using a sterile syringe to draw up and expel the diluent several times in the vial that contains the vaccine.
 - Wrap the vial in silver foil or cover it with a dark cloth. This will protect the vial from sunlight.
 - In a field situation, the vaccine or the diluent can become contaminated with dust. Cover the open top of the vial with foil to keep out dirt and flies. Clean the top of the vial with alcohol before removing the next dose.
 - Place the vaccine immediately into a cup of ice, or stand it on an ice pack. Keep the ice and vaccines in the shade.
 - Discard the reconstituted vaccine after six hours.
 - Record the dose on an immunization card for each person immunized, if it is national policy to require vaccinated persons to have a card.
 - Collect data for monitoring the activity, for example, the number of doses given. Record the number of doses given on a tally sheet so that coverage from the campaign can be calculated.
 - Remind health workers about the risk of accidental needle injuries and transmission of blood-borne diseases that can result. Review safe practices for handling and disposing of sharp instruments and needles.
 - Remind health workers that the 17D vaccine for yellow fever is very safe, and reactions to the vaccine are rare.
 - Make arrangements for safe disposal of used injection materials at the end of the activity. They can be burned or buried in a pit.
- 8) Arrange transportation to the immunization site.
- Identify the health workers and others from the health facility, district or national levels who will attend the immunization activity. Plan their transportation to and from the site.
 - Schedule vehicles and plan for fuel and other costs. Estimate per diem costs and make necessary arrangements for lodging if the site is away from the health worker's usual station.

⁴ A summary of the WHO guidelines for safe injection practices is in Annex 5.

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- 9) Communicate with community leaders about the emergency activity.
 - Request the assistance of community leaders and others who have influence in the community. Plan with them to promote the emergency activity and obtain their support.

5.4 Identify additional cases

Carry out an active search to find out if anyone else in the area around the case has been ill with the signs and symptoms that meet the case definition.

- 1) Conduct house-to-house inquiries. Talk to community health workers and traditional healers in the area. Involve community leaders who have access to the community and who may know about significant health events in the area.
- 2) Collect specimens for laboratory diagnosis from any new suspected cases. Report the results to intermediate and national levels.
- 3) Map the location of any new identified suspected cases. Use the information on the map to decide if there are areas where there are more cases occurring than in others. Look to see if travel patterns of the suspected cases have raised the potential for yellow fever transmission in areas previously not at risk. Include these areas in emergency immunization activities.
- 4) Line list the identified suspected cases.
- 5) Report case information to the next level as required normally. The national level should report the additional cases to WHO and other international health agencies as required.

5.5 Reduce mosquito breeding sites

Take steps to reduce mosquito breeding sites around the health facility and the patient's household and worksite.

- Empty water containers and clean them. Then refill them with clean water and keep the containers covered with a lid.
- Remove bottles, tyres, cut bamboo and other receptacles that collect water.

In an expanding outbreak, contact national authorities for expert advice about chemical and other methods of mosquito reduction.

5.6 Alert other areas about the confirmed outbreak

Exchange information with nearby areas about the potential for an outbreak of yellow fever in their areas. Give feedback to each level of the health system about the confirmed outbreak and the progress being made with emergency response activities. Modify activities according to local conditions or if problems occur.

Sections 5.1 through 5.6 describes immediate actions to take for responding to a confirmed outbreak of yellow fever. The next two sections describe actions that will provide a long-term affect on prevention of outbreaks in the future: routine immunizations and community education.

5.7 Include yellow fever vaccine in the routine childhood EPI schedule

In recent times, yellow fever vaccine has usually been delivered as an emergency response to an outbreak of yellow fever. Routine immunization programmes, however, can significantly reduce the threat of an outbreak and provide long-term protection against yellow fever with a single dose of 17D yellow fever vaccine.

The aim of including yellow fever vaccine in the routine schedule is to provide protection against yellow fever before an outbreak occurs. In endemic areas, especially where yellow fever has occurred in the past, a mass campaign can be conducted for the general population. Follow up the mass campaign with integration of yellow fever vaccine into the routine EPI schedule. Give yellow fever at nine months of age when the infant is brought for the measles vaccine.

Ideally, in countries where yellow fever is endemic, the entire population should be immunized against yellow fever. However, when there are limited resources, give priority to those populations at greatest risk for illness and death from yellow fever. This can be achieved by including the yellow fever vaccine in the routine childhood EPI schedule for:

- Children nine months of age. The children can receive the yellow fever vaccine at the same visit as the one for receiving a measles immunization.
- Children from six months up through fourteen years of age who live in rural areas with a high risk of yellow fever transmission. These are areas within an emerging or intermediate zone or in areas where confirmed outbreaks have already occurred.

The safe injection practices recommended for emergency yellow fever immunizations activities are also indicated for routine immunization programmes. Please refer to the recommended practices in Section 5.2.

5.8 Develop community education for prevention and control of yellow fever

Information about preventing yellow fever should be a part of primary health care programmes. Identify community leaders (especially in the areas in the district that are at risk for yellow fever) who can assist with activities for communicating prevention messages to the community. Select messages for prevention of yellow fever including the promotion of immunization with the yellow fever vaccine.

Possible health education messages are:

- Keep containers of daily water supplies covered or screened.
- Dispose of discarded waste items that could become containers for standing water (such as discarded tyres, tins, and jars.). Bury or dispose of them in a safe manner.

Involve other social agencies or institutions such as schools or religious organizations which can incorporate and promote the messages in their community health programmes.

Annexes

Annex 1	District and national level contact numbers
Annex 2	List of district reporting sites
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Annex 4	WHO Collaborating Centres for arboviruses and haemorrhagic fever reference and research (Africa, South America)
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Annex 1:

District and national level contact numbers

Record information for contacting staff responsible for yellow fever control and prevention activities at the district and national levels.

	Name and Telephone number	Facsimile number
District level staff: EPI programme manager		
Communicable disease programme manager		
Public health officer		
National level staff: EPI programme manager		
Communicable disease programme manager		
Yellow fever surveillance coordinator		
Yellow fever reference laboratory		
Other:		

Annex 2:

List of district reporting sites

Record the information for contacting the staff responsible for yellow fever control and prevention activities at reporting sites in the district.

Name of health facility	Address or location of health facility	Contact person for yellow fever surveillance	Telephone or facsimile number (or other contact information, such as e-mail)

Annex 3:

Sample case investigation form

The form on this page is the top half of the case investigation form. It can be used by health facilities as an “alert form” to guide the collection of information for the district level. *A complete case investigation form is on the next page.*

As soon as Yellow fever is suspected, contact :										
District communicable disease manager:					Telephone number: _____ Facsimile number: _____					
OR District EPI programme manager:					Telephone number: _____ Facsimile number: _____					
Patient's name and patient record number:					Sex: M [] F []					
Address:					Patient's occupation:					
District:					Village or municipality:					
State or Province:					Name of head of patient's household or village chief:					
Patient's date of birth		dd	mm	yy	Patient's age (if date of birth unknown):					
Fever (>38°C or >101°F) That did not respond to antimalarial treatment	Y	N	U	dd	mm	yy	List names of other areas or districts that patient visited during the last two weeks:			
Jaundice	Y	N	U	dd	mm	yy				
Slow pulse in relation to fever	Y	N	U	dd	mm	yy	Have cases of fever and jaundice been seen or reported in areas or districts that patient visited during the last two weeks?	Y	N	U
Bleeding from the nose, gums or skin or gastrointestinal tract	Y	N	U	dd	mm	yy				
Reduced amount of urine	Y	N	U	dd	mm	yy	Has the patient ever received at least one dose of yellow fever vaccine?	Y	N	U
Elevated level of protein in urine	Y	N	U	dd	mm	yy	What was final outcome for patient? (<i>circle one</i>) Leaving Dead Unknown If patient died, record date of death: (dd) _____ (mm) _____ (yy) _____			
Reported by: _____					Contact number for health facility: _____					

Case investigation form : suspected yellow fever

As soon as Yellow fever is suspected, contact :										
District communicable disease manager:					Telephone number: _____ Facsimile number: _____					
OR District EPI programme manager:					Telephone number: _____ Facsimile number: _____					
1. Record general information about the patient:					Date of report:					
Patient's name and patient record number:					Sex: M [] F []					
Address:					Patient's occupation:					
District: State or Province:					Village or municipality:					
Patient's date of birth					Name of head of patient's household or village chief:					
dd	mm	yy	Patient's age (if date of birth unknown):							
2. Does suspected case have:				Date of onset			3. Record travel and yellow fever immunization history.			
Fever (>38°C or >101°F) That did not respond to antimalarial treatment	Y	N	U	dd	mm	yy	List names of other areas or districts that patient visited during the last two weeks:			
Jaundice	Y	N	U	dd	mm	yy				
Slow pulse in relation to fever	Y	N	U	dd	mm	yy	Have cases of fever and jaundice been seen or reported in areas or districts that patient visited during the last two weeks?	Y	N	U
Bleeding from the nose, gums or skin or gastrointestinal tract	Y	N	U	dd	mm	yy				
Reduced amount of urine	Y	N	U	dd	mm	yy	Has the patient ever received at least one dose of yellow fever vaccine?	Y	N	U
Elevated level of protein in urine	Y	N	U	dd	mm	yy	What was final outcome for patient? (<i>circle one</i>) Living Dead Unknown If patient died, record date of death: (dd) ____ (mm) ____ (yy) ____			
Reported by: _____					Contact number for health facility: _____					

Laboratory transmittal and final classification of the case

Specimens collected (<i>Circle one</i>)	Date specimens collected (dd/mm/yy)	Date received in laboratory (dd/mm/yy)	Type of test	Results				Date results sent to MOH (dd/mm/yy)	Date results received at MOH (dd/mm/yy)
				Pos	Neg	Not processed	Unk		
Blood			IgM						
			IgG (acute)						
			IgG (convalescent)						
Malaria slide			Microscopy						
Other									
1. Were specimens or isolates sent to another laboratory? (<i>circle one</i>) Yes No Unknown				2. If YES, record laboratory's name, address, and telephone number:					
3. What is the final classification of the case? (<i>circle one</i>) Suspected Confirmed Discarded Unknown									
4. If case discarded as yellow fever, record diagnosis:				5. What was final outcome for patient? (<i>circle one</i>) Living Dead Unknown					
				6. If patient died, record date of death: (dd) ____ (mm) ____ (yy) ____					
Investigator's name: (<i>please print</i>)				Signature:					
Address:				Telephone number:					

Annex 4:

WHO Collaborating Centres for arboviruses and haemorrhagic fever reference and research

WHO Collaborating Centres for Arboviruses and Haemorrhagic Fever Reference and Research located in Africa and South America are:

Argentina	Instituto Nacional de Enfermedades Virales Humans, Dr. Julio Isidro Maiztegui, Casill de Correo 195, 2700 Pergamino. Fax: (+54) 477 7733045
Brazil	Instituto Evandro Chagas, c/o Fundacao SESP, Caixa Postal 1530, Belem. Fax: (+55) 91 2661284
Central African Republic	Institut Pasteur de Bangui, P.O. Box 923, Bangui. Fax (+236) 610109
Cuba	Instituto de Medecina Tropical, Pedro Kouri, Apartada 61, Marianoao 13, Ciudad de La Habana. Fax: (+53) 7 21957
Kenya	Kenya Medical Research Institute, Mbagathi Road, P.O. Box 54628, Nairobi. Fax: (+254) 2 725950
Nigeria	Department of Virology, College of Medicine, University of Ibadan, Ibadan. Fax: (+234) 2 413545
Puerto Rico	San Juan Laboratories, Centers for Disease Control and Prevention, 2 Calle Casia, 00921-3200 San Juan. Fax: (+1) 809 7666596
Senegal	Institut Pasteur de Dakar, 36 Avenue Pasteur, Dakar. Fax: (+221) 238772
South Africa	National Institute for Virology, Special Pathogens Unit, Private Bag X4, Sandringham 2131, Zaloska 4. Fax: (+27) 11 8820596
Uganda	Uganda Virus Research Institute, P.O. Box 49, Entebbe. Fax: (+256) 42 20631

Annex 5:

Summary of WHO policy for safe injection practices

1. Review existing injection practices to make sure health workers follow recommended practices as specified by the national policy. For example, make sure that health workers know how to:
 - Reconstitute yellow fever vaccine correctly.
 - Discard reconstituted vaccine after six hours.
 - Use safe injection practices and observe contraindications.
 - Record the dose on an immunization card.
2. Set objectives and carry out activities for improving injection practices that do not meet national policy guidelines.
3. Use injection equipment that is appropriate for each immunization setting.
4. Ensure a reliable supply of recommended equipment and supplies for providing safe injections. Monitor the reserve stock of vaccine and injection supplies to make sure an adequate amount is consistently available for meeting the needs of health facilities in your district.
5. Remind health workers about the risk of accidental needle injuries and practices for avoiding them.
6. Dispose of contaminated injection materials safely either by burning or burial.

Annex 6:

Community health education messages

This annex describes two examples of community health education messages that can be used to promote prevention and control activities. Meet with community leaders to discuss why the activities are important and decide on methods for communicating the messages to community members.

To promote an immunization activity:

Protect yourself – get immunized against yellow fever!

1. Go to _____ (*insert name of immunization site*) to get immunized against yellow fever.
2. Immunizations will be offered on _____ (*insert date*) from _____ (*insert time*) until _____ o'clock.
3. Bring your _____ (*insert type of vaccination card, EPI card, or TT immunization card used in the community*) with you, if you have one.
4. The immunizations are given for _____ (*insert information about cost, if there is one, or if the immunization is free*).

Yellow fever vaccine must be renewed every ten years for international travel.

To promote prevention activities in the community:

Yellow fever is spread by mosquitos!

You can protect yourself and your family if you:

- Cover all your water containers so mosquitos cannot breed in them.
- Look for places around buildings where mosquitos can breed. For example, look for tins, tyres, gourds and bottles that contain standing water and remove them.
- People who are ill with fever should always use a mosquito bed-net. Using a bed-net will help prevent diseases like yellow fever and malaria from spreading to others.
- A person who has a fever and yellowing of the eyes is seriously ill. Take the person to the health facility immediately.

Annex 7:

Line-listing form for suspected cases of yellow fever

This annex contains a sample line listing form for collecting data about yellow fever case investigation activities. The source of the data to include on the form is the case investigation form. Use line listing to analyse how promptly the district system is detecting and confirming suspected cases of yellow fever.

Periodically, report the information to the national level as required by national policy.

Line-listing form for suspected cases of yellow fever

District: _____ For reporting period: _____ Reported by: _____

CASE ID Nber	Name of patient (suspected case of yellow fever)	Health Facility	Received at least one dose of YF vaccine? Record Y/N	Record the patient's:		Record date specimen received in laboratory:					Record results of laboratory testing:				Record date laboratory sent results:				Record:		
				DOB (1)	Onset (2)	Acute Blood (3)	Conv Blood (4)	Liver (5)	Other (6)	IgM (7)	VI (7)	IgG (7)	Histo (7)	IgM	VI	IgG	Histo	Final Class (8)	Final Status (9)		

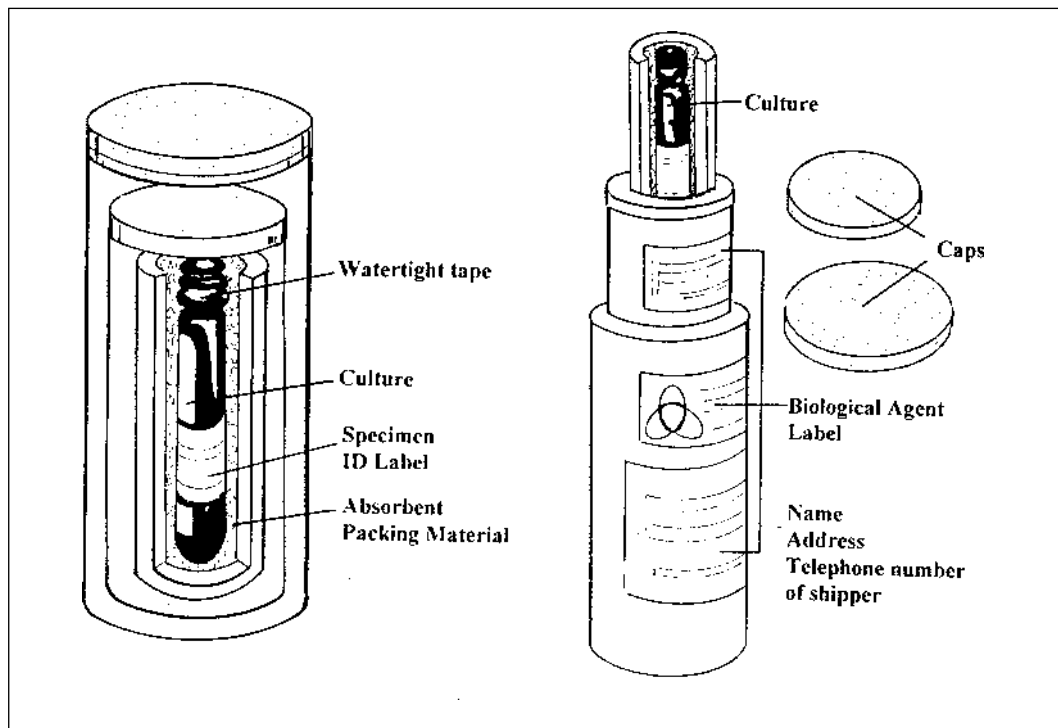
- (1) Date of birth, if known. If date of birth is unknown, record at least the year, and, if known, the month of birth.
- (2) Date of onset of first symptoms
- (3) Date first (or acute) blood sample received in laboratory
- (4) Date second (or convalescent) blood sample received in laboratory
- (5) Date liver sample received in laboratory
- (6) Date other sample received laboratory
- (7) Results of laboratory testing: Use these codes to record results: 1 = positive; 2 = negative; 3 = not done; 4 = pending; 5 = unknown
VI means 'virus isolation'. Histo means 'histopathology'.
- (8) Final classification of case. Use these codes to record the final classification: 1 = suspected case; 2 = confirmed case; 3 = discarded case; 4 = suspected case, laboratory results pending; 9 = unknown
- (9) Final status of patient. Use these codes to record the final status of patient: A = alive; D = deceased; L = lost to follow up

Annex 8:

Packaging infectious substances for air shipment

If specimens will be sent by air, they must be packed to meet international air transport (IATA) regulations.

1. The specimens must be packaged in three layers.
 - A primary water-tight container that holds the specimen.
 - A second water-tight container that holds the primary container. After the primary container is placed inside the second container, it is surrounded with absorptive material between it and the primary container so it will absorb all of the fluid in the specimen in case there is a leak.
 - An outer package which can protect the secondary package from exterior forces such as physical damage and water during transit.



-
2. The name and telephone number of the person responsible for the shipment must be marked durably and legibly on the outside of the package. One copy of the specimen data forms (case investigation form), letters, and other identification material must be attached to the outside of the second container. A copy must also be sent air mail to the receiving laboratory. A third copy will be retained by the sender.

Materials consigned in liquid nitrogen or with protection from ambient or high temperatures must be able to withstand very low temperatures; both primary and secondary packaging must be able to withstand a pressure differential of at least 95kPa and temperatures ranging from -40°C to +50°C.

3. Send a preadvice message to the consignee at least 48 hours before the package will arrive. Avoid arrival of shipments of infectious substances on weekends (either Saturday/Sunday or Thursday/Friday, depending on the destination). Send the preadvice message by telex, facsimile, or E-mail. Include the following information in the pre-advice message:
 - Place of departure
 - Place of arrival
 - Number of boxes being shipped
 - Flight number, date of arrival and the arrival time
 - Airway bill (AWB) number
 - Recommended temperature for storage of the package.
4. To facilitate formalities at customs (for both departure and arrival), complete a **proforma invoice and packing list**. Include the following information:
 - Consignee's address (the person or institution that will receive the shipment)
 - The number of boxes in the shipment
 - Details about the contents
 - Gross weight of the shipment (if necessary)
 - Value for customs formalities. (Enter a symbolic value, even for medical samples.)
 - Identifying marks
 - A short statement clarifying that the items are supplied free of charge.
5. An airway bill (AWB) must be made out by or on behalf of the shipper. The AWB is usually completed by the airline agent or the forwarding agent. It determines the contract for the carriage of specimens over the routes of the carrier. It must include the following text: **“Diagnostic specimens — Not Restricted — Packed in compliance with IATA Packing Instruction 650.”**

Annex 9:

References for further reading

Boatin, B.A., Dikassa, L., Wurapa, F.K., (1997) *Detection and control of yellow fever epidemics — a workshop for district health management team adapted materials for Interregional Training Workshop on Epidemic Preparedness*, World Health Organization, Alexandria, Egypt.

Digoutee, J., Cornet, M., Deubel, V., and Downs, W.G. (1995) “Yellow Fever” in *Exotic Viral Infections*, edited by J.S. Porterfield. Chapman & Hall, London, United Kingdom.

Field Guide for Yellow Fever Surveillance (1996) Kenya Medical Research Institute, Nairobi, Kenya.

Prevention and control of yellow fever in Africa, (1986) World Health Organization. Geneva, Switzerland.

Yellow Fever: The Immunological Basis for Immunization (1993) World Health Organization, Expanded Programme on Immunization, Geneva, Switzerland.