

# **Public health surveillance for cholera**

# Interim guidance

# February 2023

This version supersedes the 2017 GTFCC Interim guidance document on cholera surveillance

Surveillance Working Group

# Acknowledgments

Acknowledgement is given to members of the Surveillance and Laboratory Working Groups of the Global Taskforce on Cholera Control (GTFCC), experts and partners who have participated in the development of this interim guidance.

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# **Key points**

- In 2022, 30 countries across five of the six WHO regions reported cholera outbreaks, including countries which did not report cholera in previous years and countries which were not considered endemic for cholera. Many of those countries reported more cases, often with a higher case fatality ratio (CFR) than in previous years. This resurgence of the seventh pandemic of cholera further deteriorated at the beginning of 2023 (<u>Cholera Global situation, WHO, 11</u> <u>February 2023</u>). In this context, affected and at-risk countries are urged to strengthen cholera surveillance.
- This GTFCC guidance serves to provide interim recommendations for strengthening public health surveillance for cholera. This document supersedes the GTFCC interim surveillance guidance published in 2017. It provides updated recommendations on: i) case and outbreak definitions, ii) testing, in particular to expand the use of Rapid Diagnostic Tests (RDT), iii) minimum casebased data to be collected on suspected cholera cases.
- Strengthening public health surveillance for cholera in accordance with this interim guidance aims to better inform timely and targeted multisectoral interventions to limit the spread of cholera and reduce morbidity and mortality.
- Public health surveillance for cholera should include:
  - health facility-based surveillance, community-based surveillance, and event-based surveillance for the timely detection and reporting of suspected cholera cases;
  - timely reporting of standard minimum case-based data;
  - routine and systematic testing of suspected cholera cases;
  - routine analysis and interpretation of surveillance data at a fine granularity (local level);
  - regular dissemination of surveillance outputs to guide multisectoral interventions;
  - timely reporting at national, regional and global levels.
- GTFCC recommendations on environmental surveillance for cholera control are addressed in a distinct <u>Technical Note</u>.
- An updated version of this interim guidance will be published in the course of 2023.
- Questions can be directed to the Secretariat of the GTFCC (gtfccsecretariat@who.int).

# Abbreviations and acronyms

AR	Attack Rate
APW	Alkaline Peptone Water
AST	Antimicrobial Susceptibility Testing
AWD	Acute Watery Diarrhoea
AZ	Azithromycin
CFR	Case Fatality Ratio
CIP	Ciprofloxacin
GTFCC	Global Task Force on Cholera Control
IR	Incidence Rate
NA	Nalidixic Acid
NCP	National Cholera Plan
OCV	Oral Cholera Vaccination
PCR	Polymerase Chain Reaction
RDT	Rapid Diagnostic Test
TE	Tetracyclin
VC	Vibrio cholerae
WaSH	Water, Sanitation and Hygiene

# Glossary

- **Case investigation** Documentation of a suspected or confirmed cholera case in support of its classification (i.e., imported or locally acquired) to confirm or discard the occurrence of a locally acquired case indicative of a cholera outbreak. Epidemiological findings of the case investigation shall be interpreted in conjunction with microbiological results for final case and outbreak classification.
- Field investigationOn-site documentation of the epidemiological situation in time, place<br/>and person, source of exposure and risk factors for spread, to guide the<br/>response to mitigate the impact and prevent spread.
- **Immediate notification** Formalized mandatory communication process through which reportable events are communicated to the next level of the surveillance system within 24 hours.
- **Routine reporting** Process by which health events are routinely brought to the awareness of health authorities.
- Surveillance unit Lowest administrative level where decisions are taken to trigger cholera prevention and control measures and at which surveillance outputs can be used to inform local public health interventions. The corresponding administrative level is country specific. It may correspond to the scale of geographic operational units defined in a country National Cholera Plan (NCP) (e.g., commonly second-level administrative units (e.g., "counties" or "districts")) or to lower-level administrative units.
- Verification Pro-active crosschecking of the validity (veracity) of raw data or raw information related to reportable events to discard hoaxes, false rumours, and artefacts.

# I. Introduction

# 1.1 Cholera, a global threat to public health

Cholera is an acute diarrheal disease caused by ingestion of food or water contaminated with toxigenic *Vibrio cholerae* serogroup O1 or O139. The short incubation period, from a few hours to five days, may lead to an exponential rise in cases during outbreaks. While most infected people only show mild or no symptoms, some of them develop severe dehydration that can lead to death within hours if not treated.

Cholera remains a global threat to public health. It disproportionally impacts the poorest and most vulnerable populations. Areas with poor sanitation, limited access to safe water and deficient hygiene practices are at high risk for cholera transmission. In addition, limited access to health care facilities and inadequate treatment of cases are factors associated with high cholera-related mortality.

# 1.2 Importance of strengthening cholera surveillance

Cholera transmission can be ended, and the number of cholera deaths drastically reduced through targeted multisectoral interventions (Ending Cholera - Global Roadmap to 2030). These include robust community engagement, improved water, sanitation, and hygiene (WASH), oral cholera vaccines (OCV), strengthening early warning surveillance and laboratory capacities, health systems and supply readiness for early and adequate treatment, and creating rapid response teams.

Such multisectoral interventions must be guided by surveillance data at sufficient granularity, both to support the early detection and quick response to contain outbreaks and to guide the development of multisectoral strategies in National Cholera Plans (NCPs) and monitor their impact. Overall, surveillance plays a central role in providing stakeholders in other cholera prevention and control pillars with the data they need to design, implement and evaluate the impact of interventions to control cholera (Figure 1).

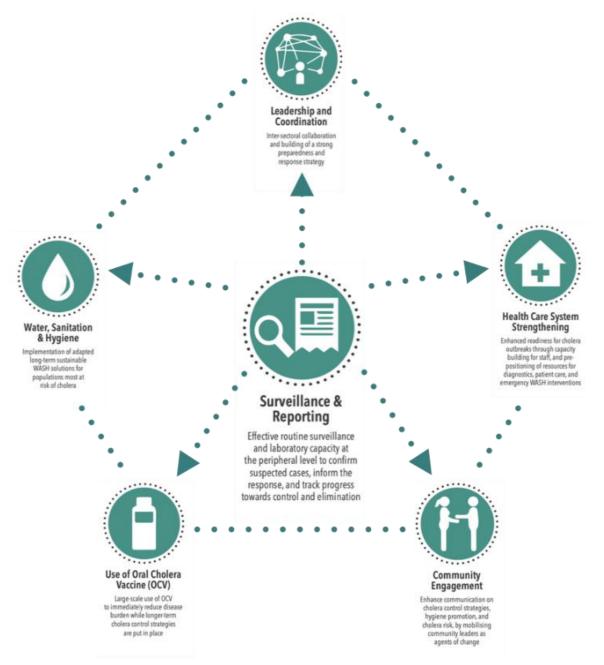


Figure 1. Multisectoral interventions for cholera control, pivotal role of surveillance

# 1.3 Objectives and target audience

This GTFCC guidance serves to provide interim recommendations to public health professionals working at Ministries of Health, Public Health Institutes, WHO Country Offices and partners for strengthening public health surveillance for cholera in the context of the resurgence of the seventh pandemic and the deterioration of the global cholera situation.

An updated version will be published in the course of 2023.

# **II. Principles**

# 1.1 Core principles

Strengthening cholera surveillance in-country should be in accordance with the following principles:

- Cholera surveillance activities should be **integrated within the existing public health surveillance system** (e.g., Integrated Disease Surveillance and Response).
- Cholera surveillance should integrate health facility-based surveillance, community-based surveillance and event-based surveillance.
- **Testing** of suspected cholera cases should be routinely undertaken in accordance with systematic testing schemes, and the use of Rapid Diagnostic Tests (RDT) should be expanded.
- Standard **case-based data** should be reported via health facility-based surveillance.
- To maximize the operational use of surveillance to inform targeted multisectoral interventions, coordination of surveillance activities and analysis and interpretation of surveillance outputs should be done at the level of **local surveillance units**.
- In each surveillance unit, surveillance modalities should dynamically adapt to the prevailing cholera situation (i.e., presence or absence of a confirmed cholera outbreak).

# 1.2 Surveillance streams

# Health facility-based surveillance

Health facility-based surveillance relies on the detection, recording and reporting by health care professionals of patients meeting standard definitions of suspected cholera cases among those who present at the health facility to seek care.

Community-Based Surveillance

Community-based surveillance relies on community health workers for the detection, reporting, and monitoring of health events in the community. It complements health facility-based surveillance by the detection and reporting of suspected cholera cases and deaths occurring in the community who are not seeking medical attention and consequently are not reported by health facilities, in particular, but not limited to, in remote areas with difficult access to health facilities. Suspected cholera cases identified through community-based surveillance should be referred to a health facility.

Detailed guidance on the design and implementation of community-based surveillance is beyond the scope of this document. Key resources are listed in Annex 1.

# Event-Based Surveillance

Event-based surveillance is a non-disease-specific surveillance method which complements surveillance efforts by capturing unstructured information from formal and informal channels, such as online content, radio broadcasts and print media, communities, health workers and laboratory workers.

Detailed guidance on the design and implementation of event-based surveillance is beyond the scope of this document. Key resources are listed in Annex 1.

# **III.** Definitions for surveillance

# 1.1 Cholera case definitions

Of note, for the purpose of community-based surveillance, it is recommended that the standard definitions listed hereafter be adapted using simplified and local language.

Acute watery diarrhoea (AWD)

Acute watery diarrhoea is an illness, where:

- Acute is defined as lasting less than seven days;
- Watery is defined as non-bloody liquid stools that may contain mucous;
- **Diarrhoea** is defined as three or more loose stools within a 24-hour period.

## Severe dehydration

A person presenting with:

- one or more of the following danger signs:
  - lethargy, loss of consciousness
  - o absent or weak pulse
  - respiratory distress

OR

- at least two of the following signs:
  - o sunken eyes
  - o unable to drink or drinking poorly
  - skin pinch going back very slowly (>2 seconds).
- Suspected cholera case
  - In surveillance units where there is no confirmed cholera outbreak

Suspected cholera case in a surveillance unit where there is no confirmed cholera outbreak

### Any person aged two years and older with acute watery diarrhoea and:

- severe dehydration
  - or
- **dying** from acute watery diarrhoea with no other specific cause attributed to this death.
  - In surveillance units where there is a confirmed cholera outbreak

Suspected cholera case in a surveillance unit where there is a confirmed cholera outbreak

Any person with or dying from acute watery diarrhoea.

### Confirmed cholera case

o In surveillance units where there is no confirmed cholera outbreak

Any person infected with *Vibrio cholerae* O1 or O139 identified by presumptive identification (culture/seroagglutination) or PCR. The strain should also be demonstrated to be toxigenic (by PCR) if there is no concomitant confirmed cholera outbreak in other surveillance unit(s) of the country and there is no established epidemiological link to a confirmed cholera case/ source of exposure in another country.

• In surveillance units where there is a confirmed cholera outbreak

Any person infected with *Vibrio cholerae* O1 or O139 identified by presumptive identification (culture/seroagglutination) or PCR.

# 1.2 Classification of cholera cases by origin of infection

As soon as a suspected or probable cholera outbreak is detected in a surveillance unit (see section on Cholera outbreak definitions), suspected cholera cases should be investigated (i.e., "case investigation" – see section on General surveillance modalities in surveillance units with absence of a confirmed cholera outbreak) for their classification by origin of infection (i.e., imported or locally acquired, Figure 2). Identification of a locally acquired cholera case is a key epidemiological criterion to determine the occurrence of a confirmed cholera outbreak in a surveillance unit.

### Imported cholera case

An imported cholera case is a suspected or confirmed cholera case infected outside of the surveillance unit where the case was detected as supported by epidemiological or microbiological evidence, or both.

#### Locally acquired cholera case

A locally acquired cholera case is a suspected or confirmed cholera case infected in the surveillance unit where the case was detected.

There are two types of locally acquired cholera cases:

- <u>import-related cholera case</u>: a locally acquired cholera case with epidemiological or microbiological evidence, or both, linking it directly to an imported cholera case or to an imported source of contamination (i.e., first-generation of local transmission).

- <u>indigenous cholera case</u>: a locally acquired cholera case with no epidemiological or microbiological evidence of a direct link to an imported cholera case or to an imported source of contamination (i.e., second or higher generation of local transmission).

Uncertainty may arise when classifying cholera cases as imported or locally acquired. Recent travel history to a country or area known to be endemic for cholera shall not be sufficient to conclude with confidence that a cholera case is an imported case. Case classification should be supported by documented evidence regarding exact dates and places visited and the prevailing cholera situation in the corresponding area(s). A conservative approach is recommended by assuming that a cholera case is locally acquired unless there is strong evidence to suggest otherwise. As a result, a cholera case with insufficient evidence to be considered an imported case should be classified as locally acquired.

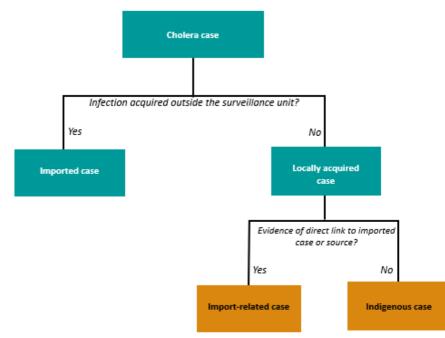


Figure 2. Flow chart for the classification in a surveillance unit of cholera cases by origin of infection

# 1.3 Cholera outbreak definitions

## • Suspected cholera outbreak

#### Suspected cholera outbreak

**Two or more suspected cholera cases** reported in the same surveillance unit within one week of each other,

or

**One person aged two years or older dying** from acute watery diarrhoea with no other specific cause attributed to this death,

or

**One confirmed cholera case pending case classification** by origin of infection (i.e., locally acquired or imported cholera case).

### Probable cholera outbreak

## Probable cholera outbreak

**The number of** suspected cholera cases with a positive **rapid diagnostic test (RDT+)** within a two-week period in a surveillance unit achieving or surpassing one of the thresholds in the Table 1 taking into account the number of suspected cholera cases tested by RDT.

# Table 1. Minimum number of suspected cholera cases tested positive by RDT for the detection of a probable cholera outbreak in a surveillance unit

Number of suspected cholera cases tested by RDT	Number of suspected cholera cases tested positive by RDT	Interpretation
Among 3 to 7 suspected cases tested	At least 3 RDT+	
Among 8 to 10 suspected cases tested	At least 4 RDT+	Probable cholera
Among 11 to 14 suspected cases tested	At least 5 RDT+	outbreak
Among 15 to 17 suspected cases tested	At least 6 RDT+	detected
Among 18 to 21 suspected cases tested	At least 7 RDT+	

Thresholds recommended in Table 1 take into account the performance of typical RDT, including the expected false positivity rate, to allow for high confidence that the positive rapid tests include at least one true cholera case. Detection of a probable cholera outbreak should trigger an extensive and comprehensive outbreak response.

### Confirmed cholera outbreak

# **Confirmed cholera outbreak**

At least one confirmed cholera case locally acquired.

### Start date of a cholera outbreak

The start date of a cholera outbreak is the date of onset of symptoms of the first locally acquired suspected cholera case detected in the surveillance unit. There is an outbreak as long as the criteria for the end of a cholera outbreak are not met.

## • End of a cholera outbreak

The criteria below for the end of a cholera outbreak apply in the presence of a well-performing surveillance system and adequate laboratory capacities for cholera testing. Where there are concerns that surveillance for cholera might lack sensitivity and/or testing for cholera might lack reliability, it is advisable to consider longer time periods.

A suspected, probable, or confirmed cholera outbreak can be considered over when for a minimum period of four consecutive weeks all suspected cases (if any) had a negative laboratory test result by culture or PCR.

In addition, the status of a probable cholera outbreak can be downgraded to a suspected cholera outbreak when all suspected cholera cases with a positive RDT result (RDT+) that triggered the probable outbreak had a negative laboratory test result by culture or PCR.

# **IV.** Surveillance objectives and general modalities

# 1.1 Surveillance objectives

Consistent with the case and outbreak definitions described in the previous section, the prevailing cholera situation in any surveillance unit at any point in time can be characterized by the presence or the absence of a confirmed cholera outbreak.

#### **Objectives**

### Surveillance units with absence of a confirmed cholera outbreak

**Rapidly detect, investigate, and respond** to any suspected or probable cholera outbreak to interrupt the onset of local cholera transmission.

### Surveillance units with a confirmed cholera outbreak

**Monitor** morbidity, mortality and affected populations to inform targeted interventions to **mitigate** the impact and spread of the outbreak and eventually **end** the outbreak.

To best serve the surveillance objectives in these two situations, some cholera surveillance modalities must adapt dynamically to the prevailing cholera situation in a given surveillance unit, in particular with regard to the applicable definition of suspected cholera cases, the recommendations for testing suspected cholera cases, and the frequency of reporting and analysis of surveillance data. This is outlined in the Table 2 and further described in the following sections.

### Table 2. Overview of surveillance modalities in surveillance units

#### with absence of a confirmed cholera outbreak and in surveillance units with a confirmed cholera outbreak

Cholera situation in the surveillance unit	Absence of a confirmed cholera outbreak	Confirmed cholera outbreak	
Objective	Rapidly detect, investigate, and respond to any suspected or probable cholera outbreak to interrupt the onset of local cholera transmission.	Monitor morbidity, mortality and affected populations to inform targeted interventions to mitigate the impact and spread of the outbreak and eventually end the outbreak.	
	Detection		
Surveillance streams			
Health facility-based	X	X	
Community-based	X	X	
Event-based	X	X	
tems under surveillance			
	Suspected and confirmed cholera cases in accordance with case definitions applicable in surveillance units where there is no confirmed cholera outbreak	Suspected and confirmed cholera cases in accordance with case definitions applicable in surveillance units where there is a confirmed cholera outbreak	
	Testing		
Frequency			
	Testing of all cholera suspected cases	Testing of a subset of cholera suspected cases according to a systematic protocol	
Methods			
RDT	All suspected cases	First 3 suspected cases per day per health facility	
Culture/PCR	All suspected cases with RDT+ (including, if warranted, PCR for toxigenicity)	3 suspected cases with RDT+ per week per surveillance unit	
Alternative if RDT not available All suspected cases tested by culture/PCR (includ warranted, PCR for toxigenicity)		First 3 suspected cases per week per health facility tested by culture/PCR	
Antimicrobial Susceptibility Testing (AST)	All confirmed case(s)	First 5 confirmed cases per surveillance unit, then a least 3 confirmed cases per surveillance unit per month	
Whole Genome Sequencing	Encouraged for confirmed imported case(s)	Encouraged on a subset of confirmed cases	
	Immediate notification		
	Any verified suspected or probable cholera outbreak	-	
	Investigation		
Case investigation	Х	-	
Field investigation	x	-	
	Data collection		
Standard minimum case- based data (health facility)	x	x	
Community-based surveillance data	х	x	
	Reporting		
	Reporting of suspected cases within 24 hours Weekly zero reporting	At least weekly - including zero reporting	
	Data analysis		
Frequency	Daily	At least weekly	
Granularity	At least at surveillance unit level	At least at surveillance unit level	

# 1.2 General surveillance modalities in surveillance units with absence of a confirmed cholera outbreak

# Detection and documentation of suspected cases

Suspected cholera cases should be routinely detected via health facility-based surveillance and community-based surveillance and documented using standard forms (see section VI. on Data collection and reporting).

## Testing of suspected cases

All suspected cholera cases should be tested (see section V. on Laboratory testing).

## Reporting, analysis, and interpretation

Minimum case-based data on any suspected cholera case(s) and RDT results should be reported within 24 hours of detection to local health authorities. It should be analysed and interpreted daily to detect any suspected or probable cholera outbreak. If no suspected cholera cases are detected, zero reporting should be done on a weekly basis.

# If a suspected or probable cholera outbreak is detected, the following key steps must be undertaken without waiting for microbiological confirmation of the outbreak.

### Verification

Verification should be completed by local health authorities within 24 hours of detection of a suspected or probable cholera outbreak. It aims to assess whether the definition for a suspected or probable cholera outbreak is met. It may include contacting the reporting source(s) or other sources (e.g., interview of clinicians or community health workers on patients' clinical presentation, case definition used, dates of onset, RDT results). A conservative approach is recommended: if a suspected or probable cholera outbreak cannot be discarded with confidence, it shall be considered verified.

### Immediate notification

A verified suspected or probable cholera outbreak should be notified to health authorities at the next level within 24 hours of verification.

# Case investigation

Case investigation should be completed by local health authorities within 24 hours of verification. It aims to gather information to classify cases by origin of infection (i.e., locally acquired or imported), identify the likely source(s) of exposure, and guide the field investigation. In addition, samples should be collected for the microbiological confirmation of cholera (if not already done).

It is recommended that case investigation be performed on all suspected cholera cases. However, if suspected cholera cases were tested by RDT and resources for investigation are limited, case investigation may be performed in priority on suspected cases with a positive RDT result (RDT+).

# Field investigation and immediate response measures

If the case investigation did not conclude with confidence that all reported cases are imported cholera cases<sup>1</sup>, field investigation should be initiated within 48 hours of verification. Field investigation aims to describe and assess the epidemiological situation and to identify the likely source(s) of exposure and risk factors for spread in order to guide immediate response measures. It should be conducted by a multidisciplinary team and combined with risk and needs assessments and immediate control measures.

<sup>&</sup>lt;sup>1</sup> Of note, if only imported cholera case(s) were detected during the case investigation, conducting active case finding is nonetheless encouraged to rule out secondary transmission. This can be achieved by contacting or visiting health facilities and community health workers to review registers and surveillance records, inquiring in the community, or conducting door-to-door screening.

Detailed guidance on field investigation, risk assessment, needs assessment, and response is beyond the scope of this document. Key resources are listed in Annex 1.

# 1.3 General surveillance modalities in surveillance units with a confirmed cholera outbreak

## Detection and documentation of suspected cases

Suspected cholera cases should be routinely detected via health facility-based surveillance and community-based surveillance and documented using standard forms (see section VI. on Data collection and reporting).

## Testing of suspected cases

The clinical management of cholera cases is based on clinical presentation, independent of laboratory confirmation or RDT result as it is primarily guided by the degree of dehydration of the patient<sup>2</sup>. Therefore, there is no need to test all suspected cholera cases in a surveillance unit with a confirmed cholera outbreak. However, some suspected cholera cases should be routinely tested to monitor the incidence of true cholera as well as microbiological characteristics (circulating strains, antibiotic susceptibility) and to eventually support the declaration of the end of the outbreak.

## Reporting, analysis, and interpretation

Routine reporting by health facilities and community health workers and data analysis by local health authorities should be performed at least on a weekly basis (see section VI. on Data collection and reporting and section VII. on Data analysis, interpretation and dissemination). However, more frequent reporting and analysis (e.g., daily) are encouraged at the onset of an outbreak and towards the end of an outbreak to help ensure timely and effective implementation of interventions to interrupt transmission.

### End of a confirmed cholera outbreak

Once the criteria for the end of a confirmed cholera outbreak are met in a surveillance unit, the prevailing cholera situation in the unit reverts to absence of a confirmed cholera outbreak and corresponding surveillance modalities apply.

<sup>&</sup>lt;sup>2</sup> Patients with a negative RDT or laboratory result should still be treated according to their symptoms.

# V. Laboratory testing

# 1.1 Capacities

# Importance

Timely, accurate, and reliable laboratory results are essential to detect probable cholera outbreaks and to confirm or discard suspected or probable cholera outbreaks, to monitor incidence of true cholera and identify the end of an outbreak, to monitor antibiotic susceptibility and to characterize circulating strains.

Laboratory testing should rely on:

- testing strategies adapted to the prevailing cholera situation at the surveillance unit level and to available resources,
- expanded RDT use to support the early detection of (probable) outbreaks and incidence monitoring,
- increased capacities for laboratory confirmation.

# Reference laboratory in country

At least one laboratory in country should be operational and capable of isolating and identifying *Vibrio cholerae* by culture or PCR and performing antimicrobial susceptibility testing. The designated reference laboratory should ensure provision of transport media and reagents, training of technicians and monitoring of the quality of testing.

# International reference laboratories

Collaboration with international reference laboratories should be established to perform quality assurance, provide training and conduct PCR testing for toxigenicity and further molecular testing for characterization and genotyping of circulating *Vibrio cholera* strains if there is no capacity to perform these such tests locally. See <u>GTFCC - Interim technical note on an introduction of DNA-based</u> identification and typing methods to public health practitioners for epidemiological investigation of <u>cholera outbreaks</u>, May 2017 and Annex 2 (List of GTFCC partners that can perform Whole Genome Sequencing (WGS)).

# 1.2 Methods

The testing algorithm most commonly used for laboratory confirmation of *Vibrio cholerae* O1/O139 is as follows: presumptive identification of *Vibrio cholerae* O1/O139 using culture and seroagglutination, and, if warranted, PCR for confirmation of toxigenicity.

Laboratories may also opt to use PCR for species identification (*Vibrio cholerae*) and serogroup identification (O1/O139) and confirmation of toxigenicity.

Other algorithms and laboratory methods may be used (such as loop-mediated isothermal amplification), however the same level of confirmation of species, serogroup and, in certain cases, toxigenicity should be maintained.

# Rapid Diagnostic Test (RDT)

RDTs are intended to be used primarily at primary health care level for surveillance purposes: as a tool for triaging samples to be further tested in the laboratories for outbreak detection in surveillance units with absence of a confirmed cholera outbreak, and to help monitor incidence trends of true cholera in surveillance units with a confirmed cholera outbreak. RDTs may also be performed within laboratories.

Testing with RDT should be performed as described in the <u>GTFCC – Job Aid Rapid Diagnostic Test</u> (<u>RDT</u>) for <u>Cholera Detection</u> and in accordance with manufacturer instructions.

False negatives using RDT can occur if specimens are collected:

- after initiating antibiotic therapy;
- in cases of poor specimen collection or handling practices (e.g., sample collected in receptacles containing chlorine residue, extended delays between collection and testing);
- when low numbers of bacteria are present in the sample (e.g., samples from patients that have been ill for longer than 4 days, or mild cases or suspected asymptomatic carriers).

# • Culture of *Vibrio cholerae*

Culture methods, including use of the chemical oxidase test and seroagglutination test with specific antisera are a quick and simple way of obtaining a presumptive identification of *Vibrio cholerae*. Recommendations for applying these methods are described in the <u>GTFCC – Job Aid Culture of Vibrio cholerae</u> and <u>GTFCC – Fact Sheet Culture of Vibrio cholerae</u>.

# Polymerase Chain Reaction (PCR)

PCR based on DNA-specific sequences unique to the pathogen provides an alternative to culture and biochemical analysis for the identification of *Vibrio cholerae* strains. Specific PCR targets for confirmation of *Vibrio cholerae* species include: *ompW*, *toxR*, *ISR*. Specific targets for confirmation of serogroup include: *rfb*O1, *rfb*O139. PCR for toxigenicity confirmation targets *ctxA*. PCR may be performed after extraction of DNA directly from stool samples, from wet or dry filter paper or cultured isolates.

For more information refer to the\_GTFCC - <u>Interim technical note on an introduction of DNA-based</u> <u>identification and typing methods to public health practitioners for epidemiological investigation of</u> <u>cholera outbreaks</u>.

# Antimicrobial Susceptibility Testing (AST)

AST is to be performed on confirmed *Vibrio cholerae* O1/O139, for minimal burden on the laboratory. AST requires capacity to culture *Vibrio cholerae*.

It is recommended to test at minimum for susceptibility to Azithromycin (AZ), Ciprofloxacin (CIP) and Nalidixic acid (NA), Tetracyclin (TE), and Trimethoprim/Sulfamethoxazole, as per the <u>GTFCC - Job Aid</u> <u>Antimicrobial Susceptibility Testing</u>.

# Whole Genome Sequencing (WGS)

WGS, as well as other advanced genotyping methods, can provide important additional information including but not limited to establishing a relationship between ongoing and previous outbreaks, tracking the genetic evolution of *Vibrio cholerae* strains and detecting the emergence of new clones, conducting phylogenetic analyses to enable the visualization of world-wide circulation and evolution of strains. It can also be used to confirm that the strains belong to the seventh pandemic El Tor lineage (7PET) if needed.

Information on WGS and other molecular typing techniques is included in the <u>GTFCC - Interim</u> technical note on an introduction of DNA-based identification and typing methods to public health practitioners for epidemiological investigation of cholera outbreaks, May 2017. See also annex 2 for a non-exhaustive list of GTFCC partners that can perform WGS.

# 1.3 Collection, packaging, transport and storage of samples

Accurate and reliable test results rely upon having a sample that has been adequately collected, stored, and transported. Methods for collection and transport of stool samples should be standardized by the reference laboratory. They should be written and available to staff or healthcare providers that collect, package, and transport samples. Results for testing for VC O1/O139 should be available within a maximum of 4 days after specimen receipt at the laboratory.

## When to collect specimens

Faecal specimens (liquid stool or rectal swabs) should be collected in the early stage of the illness, when pathogens are usually present in the stool in highest numbers, i.e., within the first four days of illness, and **before** antibiotic therapy has been initiated. However, if antimicrobial therapy has been initiated prior to sample collection, information regarding which antibiotic, dosage and duration of treatment have been prescribed should be clearly documented in the request form for laboratory testing. Antibiotic therapy may impact laboratory results, and more so culture results than RDT and PCR.

Rehydration treatment of patients should not be delayed for specimen collection. Specimens may be collected after rehydration protocols have been initiated.

## How to collect, prepare, package, store, and transport specimens

Patient stool should be collected in a clean container. The container must be clean yet free of disinfectant or detergent residue. Specimens should not be collected from bedpans as they may contain residual disinfectant or other contaminants.

If a stool specimen cannot be produced, rectal swabs may be collected.

Additional information on the procedure for sample collection may be found in the <u>CDC Job Aid –</u> <u>How to collect a fecal specimen and transfer to transport medium</u>.

Recommended methods for preparation, storage, packaging and transport of specimens are described in the <u>GTFCC - Job Aid for Specimen Packaging and Domestic Transportation</u>. The selection of the method to be used will depend on the availability of needed supplies, expected delay between sample collection and arrival at the testing laboratory, and the testing method that is to be applied to the sample in the receiving laboratory:

- A freshly collected specimen (stool or rectal swab) may be placed in a clean, well-marked (name, coordinates, type of sample, date), leak proof container and directly transported to the laboratory within 2 hours at room temperature (ideally 22-25°C). If the container must be cleaned prior to placing the sample, avoid the use of any chlorine-containing solution or disinfectant.
- 2) If a longer than 2-hour delay is expected between collection and testing, place a stoolsoaked swab into Cary-Blair transport medium. Cary-Blair transport medium is stable for long storage periods up to several months and does not require refrigeration (before use or once inoculated) if kept sterile and properly sealed.
- 3) If Cary-Blair transport medium is not available and the specimen will not reach the laboratory within 2 hours, preservation and transport of liquid stool samples on a filter paper kept in a moist environment may be an alternative. To do so, a blotting paper disc is dipped into the liquid stool and placed in a screw-cap microtube with 2 or 3 drops of normal saline solution to stop the sample from drying out. Dry filter paper can also be used for transport of faecal specimens but only for downstream DNA detection by PCR. Neither culture nor testing with RDT will be possible from a specimen on dry filter paper.
- 4) A sample of stool may also be transferred into an enrichment media called Alkaline Peptone Water (APW). APW will improve the chances of isolating *V. cholerae* when only few organisms are present in the initial sample (e.g., convalescent patients, patients that have been ill for longer than 4 days, mild cases or suspected asymptomatic carriers), or when high numbers of competing organisms are present (coinfections) or after particularly difficult transport conditions. The specimen should not exceed a volume greater than 10% of that of the volume of APW.

In any case:

- cold storage of the samples should be avoided, as this can greatly decrease the populations of *Vibrios* present in the sample and affect the quality of the laboratory results potentially leading to false negative reports. Ideally preserve samples at 22-25°C
- do not allow the specimens to dry. Add a small quantity of sterile normal saline if necessary.
- specimens should be transported in a well-marked, leak proof container appropriately packaged following local requirements and regulations for category B biological substances.

All specimens should be accompanied by a laboratory request/referral form containing at minimum the following type of information: referring facility and contact information, unique patient identifier, patient name, date of collection and conditioning of sample, type of sample, date of onset of symptoms, symptoms, geographic information about where the patient developed the first symptoms or contracted the disease, if antibiotic therapy has been initiated, RDT results if performed and type of testing requested. A template of laboratory request form for stool sample is provided in Annex 3.

# 1.4 Recommendations for testing in surveillance units with absence of a confirmed cholera outbreak

## Overview

Table 3 summarizes recommendations for cholera testing in surveillance units with absence of a confirmed cholera outbreak.

Where available, it is recommended that RDT be used in all suspected cholera cases for the early detection of a probable cholera outbreak as well as to triage RDT+ samples for further laboratory testing.

Samples for laboratory testing should be sent immediately/as soon as possible to the reference laboratory for culture or PCR confirmation, determination of serotype/biotype and antibiotic susceptibility.

Absence of a confirmed cholera outbreak			
RDT	Test all suspected cholera cases by RDT		
Laboratory testing (culture/PCR)	Test <b>all suspected cases with RDT+</b> results by culture/PCR testing including, if warranted, testing for toxigenicity		
Alternative Laboratory testing (culture/PCR) if RDT not available	Test <b>all suspected cases</b> by culture/PCR including, if warranted, testing for toxigenicity		
AST	Perform AST on <b>confirmed</b> cholera case(s)		
WGS	WGS is <b>encouraged</b> for confirmed imported cholera case(s) with uncertainty about the origin of importation if access to WGS is available but not required for public health intervention		

#### Table 3. Summary of recommendations for cholera testing in surveillance units with absence of a confirmed cholera outbreak

## Recommendations for testing where RDT are available

## o RDT use

All suspected cholera cases should be tested using RDT, and data on suspected cases and RDT test results should be reported within 24 hours of detection of any suspected cases to health authorities using standard forms (see section VI. on Data collection and reporting).

• Laboratory testing of RDT+ samples

All RDT+ samples should be tested by:

- culture and seroagglutination for presumptive identification of species (*Vibrio cholerae*) and serogroup (O1/O139) and, if warranted, PCR for confirmation of toxigenicity or
- PCR for species identification (*Vibrio cholerae*) and serogroup identification (O1/O139) and, if warranted, confirmation of toxigenicity.

Confirmation of toxigenicity in this setting, if warranted (i.e., if there is no concomitant confirmed cholera outbreak in other surveillance unit(s) of the country and there is no established epidemiological link to a confirmed cholera case / source of exposure in another country), is only to be conducted on a first confirmed case in the country.

Recommendations for testing where RDT are not available

All suspected cholera cases should be tested by:

- culture and seroagglutination for presumptive identification of species (*Vibrio cholerae*) and serogroup (O1/O139) and, if warranted, PCR for confirmation of toxigenicity or
- PCR for species identification (*Vibrio cholerae*) and serogroup identification (O1/O139) and, if warranted, confirmation of toxigenicity.
- Antimicrobial Susceptibility Testing

Perform AST on confirmed VC O1/O139 case(s).

Whole Genome Sequencing

If access to WGS is available, whether in country or through collaboration with an international reference laboratory, WGS can be used to confirm that the strain belongs to the seventh pandemic El Tor lineage (7PET) when there is no established epidemiological link to a confirmed cholera case/ source of exposure. However, it is not necessary for public health intervention or action. Samples may be preserved for WGS to take place at a later time.

# 1.5 Recommendations for testing in surveillance units with a confirmed cholera outbreak

### Overview

Table 4 summarizes recommendations for cholera testing in surveillance units with a confirmed cholera outbreak.

The number of samples collected and tested at the laboratory shall depend on the laboratory capacity as well on the outbreak dynamics in the surveillance unit considered.

Ideally, on a routine basis, a minimum of 3 samples (from suspected cases and, when available, preselected by a positive RDT) per week per health facility should be sent for laboratory confirmation and antimicrobial susceptibility testing.

Towards the end of an outbreak, testing all suspected cases by culture/PCR is recommended to confirm the end of the outbreak.

### Table 4. Summary of recommendations for cholera testing in surveillance units with a confirmed cholera outbreak

Confirmed cholera outbreak			
RDT	Test the first 3 suspected cases per day per health facility by RDT		
Laboratory testing (culture/PCR)	<b>Test 3 RDT+ per week per surveillance unit</b> by culture/PCR (without testing for toxigenicity)		
Alternative Laboratory testing (culture/PCR) if RDT not available	Test the <b>first 3 suspected cases per week per health facility</b> by culture/PCR (without testing for toxigenicity)		
AST	Perform AST on <b>first 5</b> confirmed cholera cases per surveillance unit Then, perform AST on at least <b>3</b> confirmed cholera cases per surveillance unit <b>per month</b>		
WGS	Performing WGS on a subset of confirmed cholera cases is <b>encouraged</b> if access to WGS is available but not required for public health intervention		

# Recommendations for testing where RDT are available

# o RDT use

In each health facility of the surveillance unit, the first three (3) suspected cholera cases detected each day should be tested by RDT.

If fewer than three (3) suspected cases are detected in a health facility on a given day, all suspected cases should be tested by RDT.

If RDT supply does not allow for testing three (3) suspected cases per day per health facility, the maximum number of suspected cases that can be tested per day per health facility on a consistent basis should be tested by RDT (e.g., the first suspected case per day or the first two suspected cases per day).

# • Laboratory testing of RDT+ samples

Three (3) RDT+ samples per week per surveillance unit should tested by:

- culture and seroagglutination for presumptive identification of species (*Vibrio cholerae*) and serogroup (O1/O139)
  - or
  - PCR for species identification (Vibrio cholerae) and serogroup identification (O1/O139)

Of note, toxigenicity having been already confirmed on the first positive case when the outbreak was detected in country, there is no need for further toxin testing.

If fewer than three (3) suspected cases are detected in a surveillance unit on a given week, all suspected cases should be tested.

Selection of RDT+ samples for further laboratory testing should have the goal of testing from all affected geographic areas and from multiple timepoints.

# Recommendations for testing where RDT are not available

The first three (3) suspected cases per week per health facility should be tested by:

- culture and seroagglutination for presumptive identification of species (*Vibrio cholerae*) and serogroup (O1/O139)
  - or
  - PCR for species identification (Vibrio cholerae) and serogroup identification (O1/O139)

Of note, toxigenicity having been already confirmed on the first positive case when the outbreak

was detected in country, there is no need for further toxin testing.

If fewer than three (3) suspected cases are detected in a health facility on a given week, all suspected cases should be tested.

# Antimicrobial Susceptibility Testing

At the onset of a confirmed cholera outbreak, AST should be performed on the first five (5) confirmed VC O1/O139 per surveillance unit.

Then, AST should be performed on at least three (3) confirmed cholera cases per surveillance unit per month.

If fewer than three (3) cases are confirmed in a surveillance unit on a given month, AST shall be performed on all confirmed cases.

## Whole Genome Sequencing

If access to WGS is available, whether in country or through collaboration with an international reference laboratory, the characterization of the strains on a subset of confirmed cholera cases is encouraged. However, it is not necessary for public health intervention or action. Samples may be preserved for WGS to take place at a later time.

# VI. Data collection and reporting

# 1.1 Data collection

# Health facility-based surveillance

The minimum standard case-based data listed in Table 5 should be recorded for all patients meeting the applicable definition of cholera suspected cases presenting at a health facility (regardless of the prevailing cholera situation). It can be recorded, preferably in an electronic format, in a standard register of cases (line list) or in a case report form. A template of a case report form is provided in Annex 4.

Table 5. Minimum standard cas           Information         Variable		Description				
information	Valiable	General information	List			
Date of case						
Date of reporting DateReport		reporting	DATE (dd-mm-yyyy)			
-		Name of the				
Health facility	Facility	reporting health	TEXT			
		facility				
	[	1. Patient informati	on			
Unique identifier	RecordID	Unique case identifier	TEXT			
		First name of the				
First name	FirstName	case	TEXT			
Last name	LastName	Last name of the	ТЕХТ			
Last name	Lastinallie	case				
Age in years	Age	Age of case in years	NUM			
Sex	Sex	Sex at birth of the	Female     Male			
		case Admin level 1 (e.g.,	□ Male			
		region or province)				
Admin 1 of residence	Admin1	of residence of the	TEXT			
		case				
		Admin level 2 (e.g.,				
Admin 2 of residence	Admin2	district) of	ТЕХТ			
		residence of the case				
		Admin level 3 (e.g.,				
	Admin3	health area or				
Admin 3 of residence		commune) of	TEXT			
		residence of the				
		case				
		Admin level 4 (e.g.,				
Admin 4 of residence	Admin4	ward, municipality sector or village) of	ТЕХТ			
Admin 4 of residence	Admini	residence of the				
		case				
		Address				
		complement of the				
Address of residence	Address	case	TEXT			
		(neighbourhood, street, house)				
	<u> </u>	2. Clinical informati	ion			
		Date the case				
Date of visit	DateOfVisit	consulted or was	DATE (dd-mm-yyyy)			
Date of visit	Dateorvisit	admitted at health				
		facility				
		Date the case had the first symptoms				
Date of symptom onset	DateOfOnset	of acute watery	DATE (dd-mm-yyyy)			
		diarrhoea				
		Has the case been				
		hospitalized (i.e.,	□ Yes			
Hospitalization	Hospitalization	admitted to health	□ No			
		facility for at least	Unknown			
Level of		one night)? What was the level	□ None (Treatment plan A)			
dehydration/Treatment	Dehydration	of dehydration of	<ul> <li>Mild (Treatment plan A)</li> <li>Mild (Treatment plan B)</li> </ul>			
plan	,	the case at	□ Severe (Treatment plan C)			

### Table 5. Minimum standard case-based data to be collected on suspected cholera cases

		admission or treatment plan? Treatment plan A - rehydration with ORS, no admission Treatment plan B - rehydration with ORS, admission Treatment plan C - administration of IV fluids. <sup>3</sup>	□ Unknown
Outcome	Outcome	What is the outcome of the case?	<ul> <li>Alive</li> <li>Died at health facility</li> <li>Dead on arrival at health facility</li> <li>Died in the community</li> <li>Unknown (lost to follow up)</li> </ul>
Date of outcome	DateOfOutcome	Date in which the case was discharged (if alive) or date of death (if died)	DATE (dd-mm-yyyy)
		3. Cholera testing	
Specimen collected	Specimen	Was a specimen collected for cholera testing?	□ Yes □ No
Date of specimen collection	DateOfSpecimen	If a specimen was collected for cholera testing, date of collect	DATE (dd-mm-yyyy)
RDT result	RDT	What was the result of the RDT test?	<ul> <li>Positive O1</li> <li>Positive O139</li> <li>Negative</li> <li>Inconclusive</li> <li>Not performed</li> </ul>
Specimen sent to laboratory	SpecimenToLab	Was a specimen sent to the laboratory for culture/PCR testing?	□ Yes □ No □ Unknown
Culture and seroagglutination result	CultureSeroagg	What was the result of culture and seroagglutination?	<ul> <li>Positive O1</li> <li>Positive O139</li> <li>Negative</li> <li>Inconclusive</li> <li>Not performed</li> </ul>
PCR result: serogroup	PCRSerogroup	What was the result of PCR for the serogroup?	<ul> <li>Positive O1</li> <li>Positive O139</li> <li>Negative</li> <li>Inconclusive</li> <li>Not performed</li> </ul>
PCR result: toxigenicity	PCRToxigenicity	What was the result of PCR for toxigenicity?	<ul> <li>Toxigenic</li> <li>Nontoxigenic</li> <li>Inconclusive</li> <li>Not performed</li> </ul>

<sup>&</sup>lt;sup>3</sup> For more information on treatment plan refer to Global Task Force on Cholera Control. Cholera outbreak response - field manual. Section 7: Case Management in Treatment Facilities. 2019. Available at: <u>https://choleraoutbreak.org/book-page/section-7-case-management-treatment-facilities</u>

# Case investigation

In addition to the minimum standard case-based data collected for all suspected cholera cases, additional information should be collected during case investigation when a suspected or probable cholera outbreak is detected in support of the classification of cases by origin of infection (i.e., locally acquired or imported), exploration of likely source(s) of exposure and directions for field investigation (see section on General surveillance modalities in surveillance units with absence of a confirmed cholera outbreak).

At minimum, the following should be documented:

- Travel history outside the usual place of residence in the 5 days preceding symptom onset, including dates of travel and places visited;
- Living in displacement camps/refugee camps;
- Exposure to unprotected or untreated water sources;
- Professional activity.

## Community based surveillance

Daily numbers of suspected cholera cases and cholera deaths occurring in the community (by age group of relevance for the detection of a suspected cholera outbreak (i.e., <2 years old and  $\geq$ 2 years old) should be recorded in all surveillance units (regardless of the prevailing cholera situation). If RDT testing is undertaken by community health workers, daily numbers of suspected cholera cases tested and results should also be recorded. In addition, cases identified through community-based surveillance should be referred to a health facility and reported through the facilities data stream.

A template of community-based surveillance form is provided in Annex 5.

# 1.2 Reporting

### Surveillance units with absence of a confirmed cholera outbreak

In surveillance units with absence of a confirmed cholera outbreak, the detection of cholera suspected case(s) (including those with a positive RDT result, a negative RDT result, or not tested by RDT) should be reported within 24 hours to local health authorities using the standard data collection process described in the previous section for health facility-based surveillance and community-based surveillance (Annex 4, Annex 5). In addition, if no suspected case(s) are detected, weekly zero reporting should be performed.

### Surveillance units with a confirmed cholera outbreak

In surveillance units with a confirmed cholera outbreak, reporting to local health authorities using the standard data collection process described in the previous section for health facility-based surveillance and community-based surveillance should be performed at least on a weekly basis and include zero reporting. More frequent reporting (e.g., daily) is encouraged at the onset of an outbreak and towards the end of an outbreak.

Of note, if under exceptional circumstances, reporting of minimum standard case-based data cannot be sustained in a timely manner via established channels due to outstretched capacities, aggregated reporting may be considered. Reporting of minimum standard case-based data should then be resumed as soon as possible.

### Laboratory results

Laboratories should routinely report to local health authorities (and to the health facilities where samples were collected), case-based data on samples received, tested, and test results (both positive and negative) by type of test (i.e., RDT, culture and seroagglutination, PCR, toxigenicity). Additionally, information regarding the antimicrobial susceptibility profile should be also reported to guide the case management and treatment of patients.

Case-based epidemiological data and microbiological data should be merged. If a joint electronic information system is available for health facilities and laboratories, laboratory results will be automatically updated in the health facility records. Otherwise, laboratory results should be manually recorded.

# Reporting to upper levels

Data reported through different reporting streams should be consolidated, cleaned and transmitted to the upper level of the surveillance system (Figure 3).

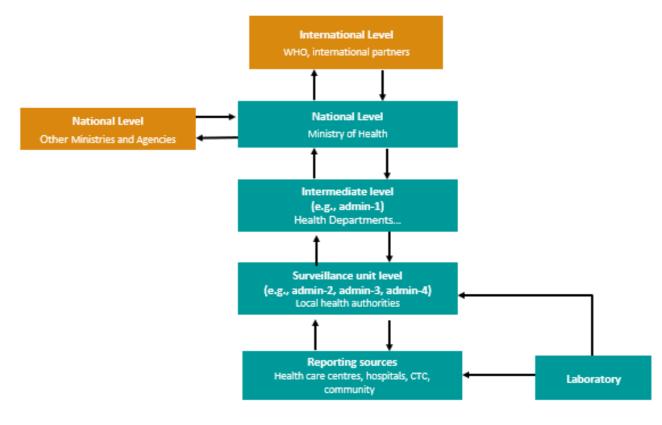


Figure 3. Information flow

# VII. Data analysis, interpretation and dissemination

# 1.1 Principles

Effective cholera surveillance is dependent on timely and systematic data analysis, interpretation, and dissemination of outputs at predefined frequency.

Data reported through the different surveillance streams should be consolidated, cleaned, analysed, and interpreted at each level of the surveillance system to inform public health interventions.

To maximize the operational use of cholera surveillance, data analysis at the level of surveillance units is of particular relevance to ensure contextually appropriate interpretations are drawn and prompt action is triggered.

Outcomes should be summarized in a situation update or epidemiological bulletin disseminated to decision-makers and relevant stakeholders at local, national, and international level (i.e., health professionals and health authorities, other relevant ministers, or agencies such as Water and Sanitation, Environmental, and international organizations and networks).

# 1.2 Surveillance units with absence of a confirmed cholera outbreak

Data analysis should be performed daily by local health authorities to detect any suspected or probable cholera outbreak.

# 1.3 Surveillance units with a confirmed cholera outbreak

Data analysis should be conducted at least on a weekly basis. More frequent reporting (e.g., daily) is encouraged at the onset of an outbreak and towards the end of an outbreak.

Data analysis should be primarily at the level of the surveillance unit, and where possible, disaggregated at lower level (e.g., health facility catchment areas) to inform targeted interventions.

Analysis should be for the latest epidemiological week and cumulatively starting from the start of the calendar year (or the start date of the outbreak). Weekly values should be compared to the previous week(s).

# Description of cases and deaths by person, place, and time

The following key figures should be monitored:

- number of suspected cholera cases;
- number of suspected cases tested by RDT/culture/PCR;
- number of cases tested positive by of RDT/culture/PCR;
- number of cholera deaths that occurred in health facilities;
- number of cholera deaths reported in the community and of deaths on arrival at health facilities;
- number of cholera cases stratified by age groups, sex, RDT result, culture and PCR result (the following age groups can be considered: <2, 2-4, 5-14, 15-44, 45-59, ≥60 years);</li>
- number of cholera deaths that occurred at health facility stratified by age groups, sex, RDT result, culture and PCR result (the following age groups can be considered: <2, 2-4, 5-14, 15-44, 45-59, ≥60 years);</li>
- proportion of cases hospitalised;
- proportion of cases by level of dehydration/treatment plan.

Analysis of the spatial distribution of cases and deaths by surveillance unit aims to describe the geographic extent of the outbreak, identify higher risk areas and populations, and formulate hypothesis regarding potential source(s) of exposure. It is recommended to include other geographic variables or points of interest that might be associated with cholera transmission (e.g., water

sources, major transportation routes, markets, etc.).

Cases and deaths can be plotted over time to monitor the outbreak dynamics (i.e., epidemic curve of the number of cases by date of onset or date of consultation/admission).

Key morbidity and mortality indicators

Key morbidity and mortality indicators to be monitored weekly are listed in the Table 6.

Population figures aim to assess the number of persons at risk and are necessary to calculate incidence and attack rates. These should be at least at the level of the surveillance unit (or lower level if available).

Morbidity and mortality indicators can be stratified by age group (e.g., at the very minimum <5 and  $\geq$ 5 years), sex, and fine geographic scale to provide further insights regarding population groups and areas at risk.

# Table 6. Key epidemiological indicators for cholera surveillance in surveillance units with a confirmed cholera outbreak

Indicator	Definition	Numerator	Denominator	Interpretation
Incidence rate (IR)	Occurrence of new cholera cases reported in a population during a given time interval. Often expressed as a rate per 1,000, 10,000 or 100,000.	Number of new cholera cases reported during a given time interval	Average population at- risk during the same time interval	Indicates the evolution of the outbreak and the rapidity of its spread and allows comparison between geographic units
Attack rate (AR) (or cumulative incidence rate)	Proportion of the population at-risk that has contracted cholera during a given time interval. Often expressed as a percentage (%).	Total number of cholera cases reported since the beginning of the outbreak	Population at risk at the beginning of the outbreak	Indicates the impact of the outbreak in the population.
Case fatality ratio (CFR)	Proportion of cholera deaths among cholera cases presenting at health facilities during a specified time interval. Often expressed as a percentage (%).	Number of cholera deaths that occurred at health facilities reported during a given time interval	Number of cholera cases reported at health facilities within the same time interval	CFR is an indicator of adequate case management and access to cholera treatment. A high CFR (≥1%) is usually due to one or a combination of different factors such as poor access to the health treatment facilities and inadequate case management.
Test positivity rate (RDT and culture/PCR)	Proportion of tests performed (RDT or culture/PCR) that are positive. Expressed as a percentage (%).	Number of positive test results (RDT or culture/PCR)	Number of tests performed (RDT or culture/PCR)	To be triangulated with the epidemic curve to support the interpretation of epidemic trends. For example, a low test positivity rate combined with an increase in suspected cholera cases may indicate a concurrent outbreak of diarrheal illness caused by a different pathogen or issues with laboratory confirmation.

# Data visualization and interpretation

Outputs should be presented in concise summary tables, graphs (e.g., age-sex pyramids, pie charts, histograms, line charts), and maps to ensure that the information is clear and understandable to non-technical staff.

Data (e.g., cases, deaths, incidence rate, case fatality ratio, samples tested, test positivity rate) can

be plotted over time to form time-trend histograms or line charts. Weekly epidemic curves are the main visual tool to establish the distribution of the number of cases (by date of onset or date of consultation/admission) over time. Important dates can be indicated alongside the epidemic curve to facilitate the interpretation of outbreak dynamics (e.g., date of the first case reported, changes in surveillance, declaration of the outbreak, response efforts including OCV campaigns, etc.).

Findings of data analysis should be interpreted to be comprehensible by stakeholders and useful for public health actions. Interpretation focuses on why the observed cholera patterns have occurred, and what this implies for interventions. Interpretation should consider contextual information that might explain the trends in indicators, risk factors, and areas and populations at-risk (such as, behavioural practices, preventative measures, social and community dynamics, seasonality, climate).

Analysis and interpretation of surveillance data should be disseminated in weekly epidemiological reports distributed among health authorities, health professionals, and other sectors (e.g., Water and Sanitation, Environmental, etc.) to inform decisions and actions for cholera multisectoral control and response interventions. A weekly national bulletin should also be shared with regional and international organizations and networks, and to other countries in particular when there is a risk of cross-border spread.

# VIII. Annexes

## Annex 1. Resources

#### • Online trainings on cholera

World Health Organization. OpenWHO - Open Course on cholera, Introduction (<u>Arabic</u>, <u>English</u>, <u>French</u> <u>Portuguese</u>, <u>Hausa</u>, <u>Pashto</u>, <u>Urdu</u>)

World Health Organization. OpenWHO - Open Course on cholera, Cholera Outbreaks: Emergency Preparedness and Response (English)

#### Cholera control and response

Global Task Force on Cholera Control. Cholera outbreak response - field manual. 2019. Available at: <a href="https://www.gtfcc.org/wp-content/uploads/2020/05/gtfcc-cholera-outbreak-response-field-manual.pdf">https://www.gtfcc.org/wp-content/uploads/2020/05/gtfcc-cholera-outbreak-response-field-manual.pdf</a> or <a href="https://choleraoutbreak.org/">https://choleraoutbreak.org/</a>

Global Task Force on Cholera Control. Cholera App. Available at: <u>https://www.gtfcc.org/cholera-app/</u>

Global Task Force on Cholera Control. Ending cholera - A global roadmap to 2030. Available at: <u>https://www.gtfcc.org/wp-content/uploads/2019/10/gtfcc-ending-cholera-a-global-roadmap-to-2030.pdf</u>

Global Task Force on Cholera Control. Interim guiding document to support countries for the development of their National Cholera Plan, August 2020. Available at: <u>https://www.gtfcc.org/wp-content/uploads/2020/11/gtfcc-interim-guiding-document-to-support-countries-for-the-development-of-their-national-cholera-plan.pdf</u>

World Health Organization. Early warning alert and response (EWAR) in emergencies: an operational guide. Available at: <u>https://www.who.int/publications/i/item/9789240063587</u>

#### Testing for cholera

CDC. Job Aid - How to collect a fecal specimen and transfer to transport medium. Available at: <u>https://www.cdc.gov/cholera/pdf/englishjobaid-stool-col-to-caryblair2.pdf</u>

Global Task Force on Cholera Control. Job Aid - Specimen packaging & domestic transportation for laboratory confirmation of Vibrio cholerae O1/O139. Available at: <u>gtfcc-job-aid-specimen-packaging-domestic-transportation-for-laboratory-confirmation-of-vibrio-cholerae.pdf</u>

Global Task Force on Cholera Control. Job Aid - Rapid Diagnostic Test (RDT) for cholera detection. Available at: <u>https://www.gtfcc.org/wp-content/uploads/2022/01/gtfcc-job-aid-rapid-diagnostic-test-for-cholera-</u> <u>detection.pdf</u>

Global Task Force on Cholera Control. Job Aid - Isolation and Presumptive Identification of Vibrio cholerae O1/O139 from fecal specimens. Available at: <u>gtfcc-job-aid-isolation-and-identification-of-vibrio-cholerae-from-fecal-specimens.pdf</u>

Global Task Force on Cholera Control. Isolation and Presumptive Identification of *Vibrio cholerae* O1/O139 from fecal specimen, fact sheet. Available at: <u>https://www.gtfcc.org/wp-content/uploads/2022/10/gtfcc-fact-sheet-isolation-and-identification-of-vibrio-cholerae-from-fecal-specimens.pdf</u>

Global Task Force on Cholera Control. Job Aid - Antimicrobial susceptibility testing for treatment and control of cholera. Available at: <u>gtfcc-job-aid-antimicrobial-susceptibility-testing-for-treatment-and-control-of-cholera.pdf</u>

Global Task Force on Cholera Control. Job Aid - Strain conditioning for international transportation of Vibrio cholerae O1/O139. Available at: <u>https://www.gtfcc.org/wp-content/uploads/2020/05/gtfcc-job-aid-strain-conditioning-for-international-transportation-of-vibrio-cholerae-1.pdf</u>

Global Task Force on Cholera Control. Interim technical note on an introduction of DNA-based identification and typing methods to public health practitioners for epidemiological investigation of cholera outbreaks, June 2017. Available at: <u>https://www.gtfcc.org/wp-content/uploads/2019/10/gtfcc-introduction-of-dna-based-identification-and-typing-methods-for-epidemiological-investigation-of-cholera-outbreaks.pdf</u>

Global Task Force on Cholera Control. Technical Note - Environmental Surveillance for Cholera Control, October 2022. Available at: <u>https://www.gtfcc.org/wp-content/uploads/2022/10/gtfcc-technical-note-</u>

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#### Data collection

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# Annex 2. List of GTFCC partners that can perform Whole Genome Sequencing (WGS) [non exhaustive]

Institution	Contact person
Pasteur Institute, France	Marie-Laure Quilici ( <u>guilici@pasteur.fr)</u>
Wellcome Sanger Institute, United Kingdom	Nicholas Thomson ( <u>nrt@sanger.ac.uk)</u>
National Institute for Communicable Diseases (NICD), South Africa	Anthony Smith ( <u>anthonys@nicd.ac.za)</u>
Centers for Disease Control and Prevention (CDC), USA	Maryann Turnsek ( <u>hud4@cdc.gov)</u>
Centre for Human Microbial Ecology Translational Health Science and Technology Institute, India	Thandavarayan Ramamurthy ( <u>tramu@thsti.res.in)</u>

Open list to be updated on ad-hoc basis.

For more information, please contact the GTFCC Secretariat: <u>GTFCCsecretariat@who.int</u>

# Annex 3. Template of laboratory request form for stool sample

# Laboratory request form for stool sample

Name of health care facility sending sample:

Contact person and contact information at health facility:

Unique patient identifier:

Patient name:

Date (dd/mm/yyyy) the sample was collected:

Type of sample (unpreserved stool, stool in Cary Blair, stool on wet or dry filter paper, stool in Alkaline Peptone Water):

Date (dd/mm/yyyy) of symptom onset:

Patient symptoms:

Location where patient fell ill (can be home address or different location if recent travel):

Has the patient received antibiotics (please circle one):

Yes / No

If yes, please specify which antibiotics, and when:

Was a rapid diagnostic test for cholera performed (please circle one):

Yes / No

If yes, please give result:

Tests requested (confirmation of V. cholerae, other):

Any additional information:

General information					
Date of reporting :	[_D_][_D_]/[_M_][_	M_]/[	_Y_][_Y_][_	Y_][_Y_]	
Health facility:					
		Patie	nt informat	tion	
Unique identifier					
First name					
Last name					
Age (in years)			years		
Sex	1		Female Male		
	Admin 1				
Place	Admin 2				
of	Admin 3				
residence	Admin 4				
	Address of residence				
		Clinic	al informat	ion	
Date of visit		[_D_	][_D_]/[_M	_][_M_]/[_Y_][_Y_][_Y_][_Y_]	
Date of onset of sy	mptoms			_][_M_]/[_Y_][_Y_][_Y_]	
Hospitalization			Yes No Unknown		
Level of dehydration at admission or treatment plan			Mild (Treat	tment plan A - rehydration with ORS, no admission) ment plan B - rehydration with ORS, admission) atment plan C - administration of IV fluids)	
Outcome			<ul> <li>Died at health facility</li> <li>Dead on arrival at health facility</li> <li>Died in the community</li> </ul>		
Date of outcome		[_D_	][_D_]/[_M	_][_M_]/[_Y_][_Y_][_Y_]	
		Chole	era testing		
Specimen collected	I		Yes No	If yes, date of specimen collection: [_D_][_D_]/[_M_][_M_]/[_Y_][_Y_][_Y_]	
RDT result			Positive O1 Positive O1 Negative Inconclusiv Not perforr	39 e	
Specimen sent to t	he laboratory		Yes No Unknown		
Culture and seroagglutination result			Positive O1 Positive O1 Negative Inconclusiv Not perforr	39 e	

# Annex 4. Template of a cholera case report form

	Positive O1
	Positive O139
PCR result – serogroup	□ Negative
	Inconclusive
	Not performed
	Toxigenic
PCR result - toxigenicity	Nontoxigenic
	Inconclusive
	Not performed

# Annex 5. Example of a community-based surveillance form

Surveillance unit:\_\_\_\_\_

Community/Village:\_\_\_\_\_

Date of reporting:\_\_\_\_\_

Name of community health worker:

Telephone number:

Date (DD/MM/YYYY)	Number of suspected cholera cases				Number of suspected cholera cases tested by	cholera cases tested	Number of suspected cholera cases referred to a	Comments
	<2 yro	≥2 yro	<2 yro	≥2 yro	RDT (if applicable)	positive by RDT (if applicable)	cholera treatment centre/unit	
Total								