1. BACKGROUND

REVISION OF THE GTFCC TESTING RECOMMENDATIONS

- **Global upsurge of cholera outbreaks the past year**
- **Challenges** and **limitations** of cholera surveillance, including a **low testing rate, irregular testing,** and **lack of integration of epidemiological/laboratory** data
- Provisional update of the **GTFCC Interim guidance on public health surveillance for cholera** (Feb. 2023), supersedes 2017 GTFCC interim guidance, ensuring surveillance data provide:
  - ✓ an accurate and granular picture of the cholera epidemiological situation.
  - ✓ updated recommendations on testing

English: https://tinyurl.com/SurvFeb2023

French: https://tinyurl.com/SurvFev2023

ADAPTIVE SURVEILLANCE AT THE LOCAL LEVEL

To maximize the operational use of surveillance data

Surveillance objectives and modalities are **adapted to the cholera situation at the local level**

Local level: - **surveillance unit**
- administrative unit no bigger than an NCP operational unit / country specific

Cholera situations	Surveillance objectives
Absence of a confirmed cholera outbreak	To **rapidly detect, investigate, and respond** to suspected/probable cholera outbreak **to interrupt** the onset of local transmission
Confirmed cholera outbreak	To **monitor the morbidity, mortality and affected populations** to inform targeted interventions **to mitigate the impact and spread** and eventually end the outbreak

SYSTEMATIC STRATEGIES FOR TESTING

To increase the **accuracy** of surveillance

Systematic strategies for testing adapted to the cholera situation at local level, including:

- Expanded **RDT** use for early outbreak detection and outbreak monitoring
- Alternative recommendations if RDTs are not available
- More specific recommendations for **culture** and **PCR** use

INCREASED CAPACITIES FOR LABORATORY TESTING:
EXPANDED USE OF RDT

- RDTs meeting satisfactory performance shall become more widely available
- Opportunity to reconsider the **use of RDTs to enhance the accuracy of cholera surveillance** in the short term, while increasing capacities for confirmatory testing in the longer term

- RDT are to be used primarily at primary health care level for :
  - **outbreak detection** in surveillance units with absence of a confirmed cholera outbreak
  - **monitoring incidence trends** of cholera in surveillance units with a confirmed cholera outbreak
- Tool for triaging samples to be further tested in the laboratory

INCREASED CAPACITIES FOR LABORATORY TESTING:
SYSTEMATIC IMPLEMENTATION OF CONFIRMATORY TESTS

Current Status

- Confirmation by culture is not always performed and it is necessary to clearly define what is considered as a positive culture result.
- Lab culture results are not always reported up to the national level.
- PCR has been introduced in a few laboratories although many are equipped with the necessary material. No consensus to date on the situations requiring PCR testing or on the method.

GTFCC Interim Surveillance Recommendations (Feb. 2023)

- Recommendations on the **regularity of testing** : when and how many samples for confirmation of identification/toxigenicity testing/AMR testing

2. TESTING RECOMMENDATIONS IN SURVEILLANCE UNITS WITH ABSENCE OF A CONFIRMED CHOLERA OUTBREAK

SURVEILLANCE UNITS WITH ABSENCE OF A CONFIRMED CHOLERA OUTBREAK

Surveillance objectives

To **rapidly detect, investigate, and respond** to suspected/probable cholera outbreak **to interrupt** the onset of local transmission

Testing strategy

Testing of all suspected cholera cases

SURVEILLANCE UNITS WITH ABSENCE OF A CONFIRMED OUTBREAK
RDT use – detection of probable cholera outbreak

- Thresholds are statistically determined to provide high confidence that at least one suspected case with RDT+ is indeed a true cholera case

- **Maximizes use of RDT for rapid response**

- Takes into account RDT performance (specificity)

https://www.gtfcc.org/wp-content/uploads/2022/01/gtfcc-job-aid-rapid-diagnostic-test-for-cholera-detection.pdf

SURVEILLANCE UNITS WITH ABSENCE OF A CONFIRMED OUTBREAK RDT use

- **All suspected cholera cases** should be tested by RDT
- Data (suspected cases and RDT test results) should be reported daily to health authorities to detect any **probable cholera outbreak**

Minimum nb of suspected cases RDT+ for the detection of a probable cholera outbreak in a surveillance unit

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

SURVEILLANCE UNITS WITH ABSENCE OF A CONFIRMED OUTBREAK
Culture and seroagglutination, PCR

If RDTs are used = All RDT + cases
If RDTs are not used = All suspected cases

A confirmed cholera case is any person infected with *Vibrio cholerae* O1or O139

- Identified by **culture and seroagglutination** as the minimum standard (presumptive identification)
- Confirmed as toxigenic by PCR recommended on the first **positive VC O1 or O139 sample**

Note: other methods may be used (such as loop-mediated isothermal amplification) but ensuring the same level of confirmation (species, serogroup and toxigenicity if applicable).

https://www.gtfcc.org/wp-content/uploads/2022/10/gtfcc-job-aid-isolation-and-identification-of-vibrio-cholerae-from-fecal-specimens.pdf
https://www.gtfcc.org/wp-content/uploads/2022/10/gtfcc-fact-sheet-isolation-and-identification-of-vibrio-cholerae-from-fecal-specimens.pdf

SURVEILLANCE UNITS WITH ABSENCE OF A CONFIRMED OUTBREAK SPECIFIC CONSIDERATIONS CONCERNING PCR

- *PCR testing may be performed directly on stool samples or on cultured isolates.*
- Laboratories may opt to use PCR for species (*Vibrio cholerae*) and serogroup (O1/O139) identification and confirmation of toxigenicity **as an alternative**
- Confirmation of toxigenicity is required
  - When there is no concomitant confirmed cholera outbreak or established epidemiological link to a confirmed cholera case/ source of exposure.

    (could be countries facing cholera after long periods of lull with no evident source of introduction)
  - On **the first confirmed case only** ie if *Vibrio cholerae* O1/O13 is confirmed
- If PCR is not available locally, samples should be sent to a reference laboratory for toxin testing.

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

SURVEILLANCE UNITS WITH ABSENCE OF A CONFIRMED OUTBREAK AST & WGS

Antimicrobial Susceptibility Testing

gtfcc-job-aid-antimicrobial-susceptibility-testing-for-treatment-and-control-of-cholera.pdf

- Should be performed on **all** confirmed cases

- Requires **culture capacity** in order to perform antimicrobial susceptibility testing (AST), as AST is performed on cultured isolates.
- Is to be performed on **confirmed** *Vibrio cholerae* O1/O13
- Should aim to test the antibiotics recommended for the treatment of cholera at the minimum
- If the laboratory do not have capacity to perform AST, they are requested to be able to send samples/isolates to a national reference laboratory for AST (results within 7 days).

Whole Genome Sequencing

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

- **Encouraged** to confirm a pandemic strain if there is uncertainty about the origin of the case
- Not required for Public Health intervention

SURVEILLANCE UNITS WITH ABSENCE OF A CONFIRMED OUTBREAK
Summary

	Testing	Systematic strategy
RDT available	**RDT testing**	• **All suspected** cholera cases
	Lab confirmatory testing	
	• Culture-seroagglutination or PCR for confirmation of *V. cholerae* O1 or O139	• **All RDT+** cases
	• PCR for toxigenicity	• On **the first** confirmed *V. cholerae* O1
RDT not available	**Lab testing**	
	• Culture-seroagglutination or PCR for confirmation of *V. cholerae* O1 or O139	• **All suspected** cholera cases
	• PCR for toxigenicity	• On **the first** confirmed *V. cholerae* O1
Complementary tests	**AST**	• On **all** confirmed cholera cases
	WGS	• Encouraged for confirmed imported cholera case(s) **with uncertainty about the origin of importation**

3. TESTING RECOMMENDATIONS IN SURVEILLANCE UNITS WITH A CONFIRMED CHOLERA OUTBREAK

SURVEILLANCE UNITS WITH A CONFIRMED CHOLERA OUTBREAK

Surveillance objectives

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

Testing strategy

Testing of a subset of suspected cases according to a systematic protocol

SURVEILLANCE UNITS WITH A CONFIRMED CHOLERA OUTBREAK
RDT use

On a routine basis:

- In each **health facility** of a surveillance unit, the **first 3 suspected cholera cases detected each day** should be tested by RDT
- If RDT supply does not allow for testing 3 suspected cases/day/facility, the **maximum number of suspected cases that can be tested/day/health facility on a consistent basis** should be tested by RDT

SURVEILLANCE UNITS WITH A CONFIRMED CHOLERA OUTBREAK
Culture and seroagglutination, PCR

Where RDTs are available

- At least **3 RDT+ samples per week** per health facility

Where RDTs are not available

- **First 3 suspected cases per week** per health facility

Towards the end of an outbreak

- **All** suspected cases (to confirm the end of the outbreak)

- Identification by **culture and seroagglutination** (presumptive identification) or other method ensuring the same level of confirmation

- PCR for *V. cholerae* O1/O139 identification as an alternative but **no need to confirm toxigenicity** (already confirmed on the first positive case)

- *Select RDT+ samples representative of all affected geographic areas and timepoints.*

SURVEILLANCE UNITS WITH A CONFIRMED CHOLERA OUTBREAK
AST & WGS

Antimicrobial Susceptibility Testing

- On the first 5 confirmed cases per surveillance unit
- Then, at least **3** confirmed cases per surveillance unit **per month**
  - In the beginning of a new active outbreak, there may be uncertainties regarding the origin of cases and/or epidemiological links.
  - Resistance may be acquired over time, particularly when antibiotics are used commonly.
  - New profiles could be a result of a new introduction of VC.

Whole Genome Sequencing

- **Encouraged** for longer-term studies for a subset of confirmed cases
- Not required for public health intervention

TESTING STRATEGY IN UNITS WITH A CONFIRMED OUTBREAK

Summary

	Testing	Systematic strategy
RDT available	**RDT testing**	• **The first 3 suspected cases per day** per health facility
	Lab confirmatory testing	
	• **Culture-seroagglutination or PCR for confirmation of *V. cholerae* O1 or O139**	• On **3 RDT+ per week** per surveillance unit
	• PCR for toxigenicity	• No testing for toxigenicity is required
RDT not available	**Lab testing**	
	• **Culture-seroagglutination or PCR for confirmation of *V. cholerae* O1 or O139**	• The **first 3 suspected cases per week** per health facility
	• PCR for toxigenicity	• No testing for toxigenicity is required
Complementary tests	**AST**	• On **first 5 confirmed cholera cases** per surveillance unit • Then on **at least 3 confirmed cholera cases** per surveillance unit **per month**
	WGS	• Performing WGS on a subset of confirmed cholera cases is encouraged

4. TESTING RECOMMENDATIONS NEXT STEPS

NEXT STEPS
Operationalization

- Support countries to implement the recommended testing strategies

- Address country feedback

We need to hear from you

NEXT STEPS
Improvement of recommendations

- Comprehensive update of the GTFCC guidance on cholera surveillance (by the end of 2023) will include:
  - Testing recommendations for a **comprehensive adaptive surveillance framework** (including additional cholera situations: clustered transmission and community transmission)
  - Didactic "use case" of **probable cholera outbreak** definition
  - Further **operational guidance** (e.g., inconclusive RDT result, use of RDT in the context of CBS, specimen storage, safety and quality, enriched/direct RDT)
  - Minimum **performance targets** for routine monitoring and evaluation of cholera surveillance, including testing


Thank you
Together we can
#endcholera
GLOBAL TASK FORCE ON
CHOLERA CONTROL