

# A multi-site pilot study of the deployment of cholera rapid diagnostic tests in the Democratic Republic of the Congo

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## CONTEXT

The Global Task Force for Cholera Control (GTFCC) has set an ambitious goal to eliminate cholera as a public health threat by 2030, focusing on at least 47 countries where cholera remains a significant burden, with an estimated 2.86 million cases and 95,000 deaths annually. Despite efforts, cholera surveillance faces challenges, including low specificity of case definitions and imperfect laboratory confirmation. Rapid Diagnostic Tests (RDTs) show promise but have variable performance. Integrating RDTs into surveillance systems could enhance early cholera detection, enhance monitoring and guide vaccination decision making, especially in outbreak settings. In the Democratic Republic of Congo (DRC), cholera remains a major concern, with endemic and outbreak-prone regions. This study is further investigating the integration of RDTs into routine surveillance, particularly the RDT sampling and deployment strategies in different setting with varying study team support.

### Primary objective

Derive and compare estimates of the true clinical incidence of cholera based on RDTs using different sampling schemes.

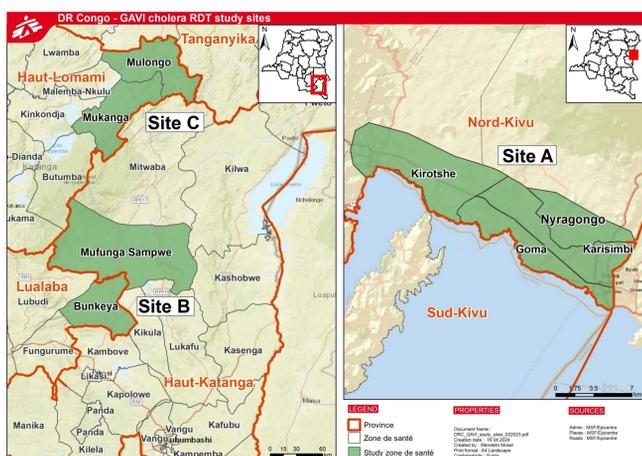
### Secondary objectives

1. Evaluate the practical use of RDTs (with and without enrichment) for surveillance in terms of compliance, timeliness of reporting at different levels, consumption, supply, and cost in sites with moderate study team support.
2. Implement a specific predefined sampling scheme in a setting with minimal study team support and evaluate compliance to application, timeliness of reporting, consumption, supply, and cost.
3. Assess the performance (sensitivity, specificity) of different cholera RDTs with and without enrichment under real-world deployment conditions.
4. Assess feasibility and acceptability of cholera RDT implementation into surveillance in sites with moderate study team support and those with minimal to no support.
5. Describe country stakeholders' views of the feasibility and use of cholera RDTs, sampling strategies, reporting of results and cholera incidence that should trigger preventive vaccination campaigns.

## METHOD

### Characteristics

- **Study period:** Mai 2023 – July 2024 (1 year data collection)
- **Funding:** GAVI
- **Type of research:** Observational and mixed methods
- **Inclusion:** Each person presenting to a CTC/UTC/CS in the study area and corresponding to the definition of a suspected cholera case.
- **Laboratory testing:** National Institute for Biomedical Research (INRB) Goma (culture site A, all qPCR), Grand Laboratoire Medical Lubumbashi (GLML, culture site B)



### Study sites

- **Site A:** (High incidence setting: ZS Goma, ZS Nyiragongo, ZS Karisimbi and ZS Kirotshe)
  - High study team support (Epicentre nurse supervisors visiting regularly all CTC/UTC)
  - Exhaustive testing of all suspect cases in the CTC/UTC with the RDT Crystal VC O1/O139 (with and without enrichment), culture and qPCR and a subset of suspect cases with the RDT SD Bioline
- **Site B:** (Low- to medium incidence setting: ZS Mufunga Sampe and ZS Bunkeya)
  - High study team support (Epicentre nurse supervisors visiting regularly all CTC/UTC)
  - Exhaustive testing of all suspect cases in the CTC/UTC with the RDT Crystal VC O1/O139 (with and without enrichment), culture and qPCR
- **Site C:** (Low- to medium incidence setting: ZS Mulongo and ZS Mukanga)
  - Real world setting (idea of minimal support to investigate the real-world deployment of RDTs)
  - Minimal study team support (training of BCZ supervisors for implementing strategies in CTC/CTU)

	Mulongo	Mukanga
<b>RDT storage</b>	Decentralized in CTC/CTU	Centralized (BCZ)
<b>Outbreak detection</b>	Testing of all suspect cases with a Crystal VC O1/O139 until GTFCC threshold for detection of a probable outbreak is reached	BCZ investigates and tests the first suspect case with a Crystal VC O1/O139. In case of a positive RDT, the BCZ starts to distribute the RDTs to all CTC/CTU
<b>Testing strategy during outbreak</b>	First 3 / day / CTC/CTU	First 3 (<5 years) and first 3 (≥5 years) / day / CTC/CTU

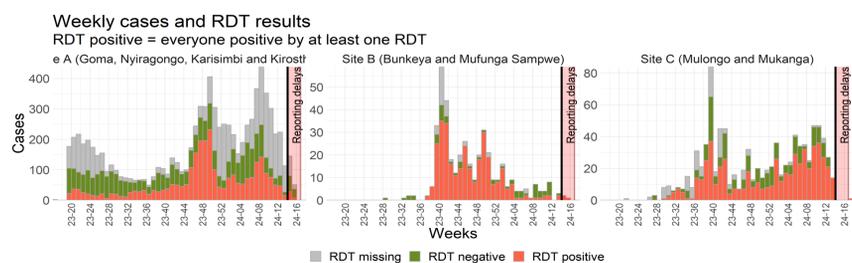
### Qualitative part

- Focus group discussions and individual interviews about the integration of the RDT in the routine surveillance system with MoH health staff involved in the study at different levels (nurses, head of health centre, head of health zone etc.)
- Individual interviews with the country's stakeholders on the feasibility and use of the cholera RDT

## RESULTS (Data collection in progress [data analysed up to the 29.04.2024]: Preliminary and Incomplete Results)

### Inclusions

Site A: 8'841, Site B: 412, Site C: 925



### RDT results and performance

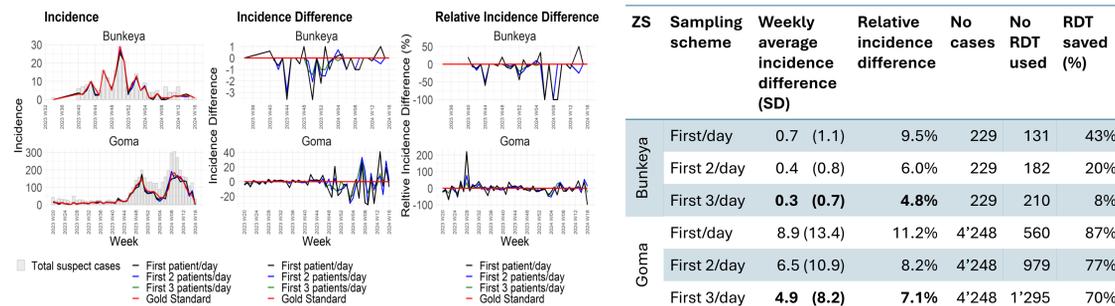
- Result of Crystal VC01/0139: 46.0% positive for 01 serotype, 6% positive for 0139 serotype and 6% for both serotypes.
- The 0139 serotype was not yet confirmed in DRC and presumably a reading error or false positive, further investigations are ongoing.
- The sensitivity compared to the gold standard (culture) was highest among all RDTs for the simple Crystal VC01/0139 with 82.2% (95%CI 81.0-83.4) and the specificity for the SD Bioline after enrichment with 75.8% (95% CI 73.9-77.6).

RDT	Enrichment	n	Sensitivity		Specificity			
			CI low	CI up	CI low	CI up		
Crystal VC0139	No	3,820	82.2	81.0	83.4	60.7	59.1	62.2
Crystal VC0139	Yes	2,922	79.6	78.1	81.0	68.5	66.8	70.2
SD Bioline	No	2,230	76.8	75.1	78.6	70.7	68.8	72.6
SD Bioline	Yes	2,015	68.1	66.0	70.1	75.8	73.9	77.6

### Identifying sampling scheme closest to reality

Which sampling scheme (e.g., testing only the first patient, the first 2 or 3 patients per day, per CTC/UTC) aligns closest with the health zone incidence rates obtained from the gold standard (exhaustive sampling of all patients)?

- Example shown: Bunkeya with low-incidence and Goma with a high-incidence



- Lowest average and relative incidence difference was found for the sampling scheme "first 3 / day" in Bunkeya and Goma.
- This sampling scheme leads to the saving of 70% of RDTs when compared to exhaustive testing in Goma (high incidence), and 8% of RDTs in low incidence (Bunkeya)
- The RDT testing strategy "first 3 patients / day / CTC/UTC was evaluated in the 12 CTC/UTC of the ZS Mulongo. The scheme was applied correctly during 83% of the 374 days with minimum one case, but only during 28% of days with >3 patients per day (n=25).

### Some RDT facts

- Average required time to conduct a RDT: 12:39 minutes (sample collection: 2:44 min; RDT preparation: 5:05 min; reading and result recording 4:50) plus 15-30 min time to wait until the result appears.
- Compliance with SOP-steps in the CTC/UTC: 83% followed correctly all 4 SOP-steps for sample preparation, 88% the 10 steps to prepare the RDT and 72% followed the 8 steps of result reading and recording.
- 0.05% of the RDTs had an inconclusive result and 0.5% were wasted in the CTCs.

## CONCLUSIONS

- A total of 10,182 suspect cases were included in the three designated sites up to April 29, 2024, with the study planned for continuation until the end of July 2024. Among all inclusions, 3'820 cases underwent testing utilizing the Crystal VC01/0139 and culture, with highest sensitivity among the array of RDTs incorporated in the study.
- RDTs have emerged as indispensable tools for cholera surveillance, especially in the context of ongoing outbreak monitoring. In the light of their considerable expense, limited shelf life, and logistical challenges, a pragmatic approach involves the selective testing of a subset of suspect cases, with resulting incidence data serving as a basis for informed decision-making. Preliminary analysis, including only three sampling schemes (with further comparisons underway), has revealed a convergence in incidence rates between exhaustive testing and the examination of solely the first three suspect cases daily per CTC.
- Applying a sampling scheme might only conserve few RDTs in low-incidence settings, however, in high-incidence settings almost two-third of the RDTs can be saved. Nonetheless, the implementation of the chosen sampling scheme necessitates close monitoring and adherence to established protocols.