GLOBAL TASK FORCE ON
CHOLERA CONTROL

REPORT OF THE

MEETING OF THE GLOBAL TASK FORCE ON CHOLERA CONTROL SURVEILLANCE

EPIDEMIOLOGY & LABORATORY WORKING GROUPS

2-5 May 2023 | Hybrid meeting

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Acronyms and abbreviations

Africa CDC	Africa Centres for Disease Control and Prevention
AST	antimicrobial susceptibility testing
AWD	acute watery diarrhoea
CBS	community-based surveillance
CDC	Centre for Disease Control, Atlanta
CFR	case fatality rate
CSP	GTFCC Country Support Platform
CTC	cholera treatment centre
DRC	Democratic Republic of Congo
EBS	event-based surveillance
Gavi	Global Alliance for Vaccines and Immunization
GOARN	Global Outbreak Alert and Response Network
GTFCC	Global Task Force on Cholera Control
icddr,b	International Centre for Diarrhoeal Disease Research, Bangladesh
ICG	International Coordinating Group
IDP	internally displaced people
IPC	infection prevention and control
IRP	Independent Review Panel
JHU	Johns Hopkins University
JMP	WHO/UNICEF Joint Monitoring Program for Water Supply, Sanitation and Hygiene
LNSP	Public Health National Laboratory of Haiti
M&E	monitoring and evaluation
MYP	multi-year plans of action
NCP	national cholera plan
OCV	oral cholera vaccine
ORP	oral rehydration point
PAHO	Pan American Health Organization
PCR	polymerase chain reaction
PFGE	pulsed-field gel electrophoresis
PQ	WHO-prequalified
RDT	rapid diagnostic test
RRT	rapid response team
SOP	standard operating procedure
TPP	target product profile
US CDC	US Centers for Disease Control and Prevention
USAID	US Agency for International Development
WASH	water, sanitation and hygiene
WGS	whole genome sequencing

Background

The Global Task Force on Cholera Control (GTFCC) Surveillance (Epidemiology & Laboratory) and Laboratory Working Groups convened in Maputo, Mozambique on 2-5 May 2023 to present their work over the preceding year.

The Epidemiology and Laboratory Workings Group meeting presented outcomes in the following areas:

- Identification of priority areas for multisectoral interventions (PAMI)
- Country-level cholera surveillance
- Regional and global cholera surveillance
- Testing and confirmation of cholera.

Additional specific outcomes of the Laboratory Working Group in the following areas were also presented:

- Testing and confirmation of cholera
- Laboratory capacity and competency.

Generously hosted by the Mozambique Ministry of Health, the meeting saw lively discussion between technical experts, GTFCC partners and country representatives as they worked together to shape the way forward through contributions to the development of guidance, standards, resources and workplans for the coming year. The goal of all this: to strengthen cholera surveillance and testing and improve the evidence base for multisectoral strategies to end cholera.

Surveillance (Epidemiology & Laboratory) working groups

The meeting opened with brief welcomes from Flavio Finger (Chair of the Epidemiology Working Group) and Marie-Laure Quilici (Chair of the Laboratory working group) and Philippe Barboza (head of the GTFCC Secretariat). They set the context of the current cholera situation and emphasized the central importance of surveillance to achieving the goals of the GTFCC Global Roadmap to End Cholera by 2020 (aka the Global Roadmap).

Opening remarks

***Armindo D. Tiago**, Mozambique Minister of Health*

The meeting was officially opened by Armindo D. Tiago, Minister of Health of Mozambique, who expressed his gratitude for the selection of Maputo as a location for the meeting. The Minister began by drawing attention to the global burden of cholera, and the discrepancy between estimates and recorded cases, which he attributed to limitations in surveillance systems.

The Minister emphasized that since mid-2021, multiple cholera outbreaks with high caseloads and fatalities have been witnessed worldwide, even in regions that had previously been cholera free. In 2022, the number of countries reporting cholera cases rose to 30, including 14 that had not recorded the disease in the previous year. Distressingly, in the first two months of 2023, 22 countries reported outbreaks.

Within Mozambique, cholera has historically been endemic in certain regions, with periodic outbreaks in localized areas. However, the situation has changed significantly in recent months, and since September 2022 the country has faced a major epidemic, spreading to 10 out of the 11 provinces and affecting 56 districts. So far, Mozambique has reported a cumulative total of 28 830 cases and 127 deaths, marking its largest cholera epidemic in the past two decades. The Minister attributed the resurgence of cholera to several factors, including extreme weather events exacerbating poor sanitation conditions, limited access to safe drinking water, population mobility, and other sociocultural factors.

The Minister highlighted the actions that his government has implemented in response to the ongoing epidemic, including expanding access to potable water, distributing water purification products, conducting educational and social mobilization campaigns to promote disease prevention practices, and providing training for healthcare professionals. The health sector has also strengthened epidemiological surveillance, expanded laboratory testing capabilities, implemented a differentiated approach for case management, and administered vaccines through reactive vaccination campaigns in heavily affected regions. To date, over 2.4 million people have been vaccinated in six provinces. These efforts have yielded positive results, with a noticeable improvement in the epidemiological situation in recent weeks, but the Minister cautioned against complacency and emphasized the need to sustain response actions as significant transmission foci persist in various parts of the country.

The Minister echoed the call for increased availability and accessibility of cholera vaccines globally, underscoring the positive impact of vaccination in conjunction with other preventive measures. Mozambique is in the advanced stages of drafting a National Cholera Plan (NCP) for the Elimination of Cholera, which will consolidate a multisectoral preventive approach to the disease. The plan is expected to be submitted for government approval in the latter half of 2023.

Mozambique is proud of its representation on the GTFCC, and the Minister expressed hope that this meeting would strengthen collaborative networks for cholera prevention and response. In conclusion, he voiced the hope for an open and productive discussion, with a particular emphasis on addressing Mozambique's challenges.

Cholera in Mozambique

JP Langa, *Mozambique Ministry of Health*

Dr Langa supplemented the Minister's overview of the cholera situation in Mozambique with an epidemiological overview. The country reported 29 280 cases with 131 deaths (CFR: 0.4%). 18,872 had been hospitalized.

Cholera in Mozambique has tended to be highly seasonal and focussed on a small number of vulnerable provinces, with Zambézia, Sofala, Niassa and Tete particularly affected.

Dr Langa gave a brief overview of Mozambique's cholera control and monitoring efforts, which have been hampered by a delicate security situation of the north of the country.

Identification of priority areas for multisectoral interventions

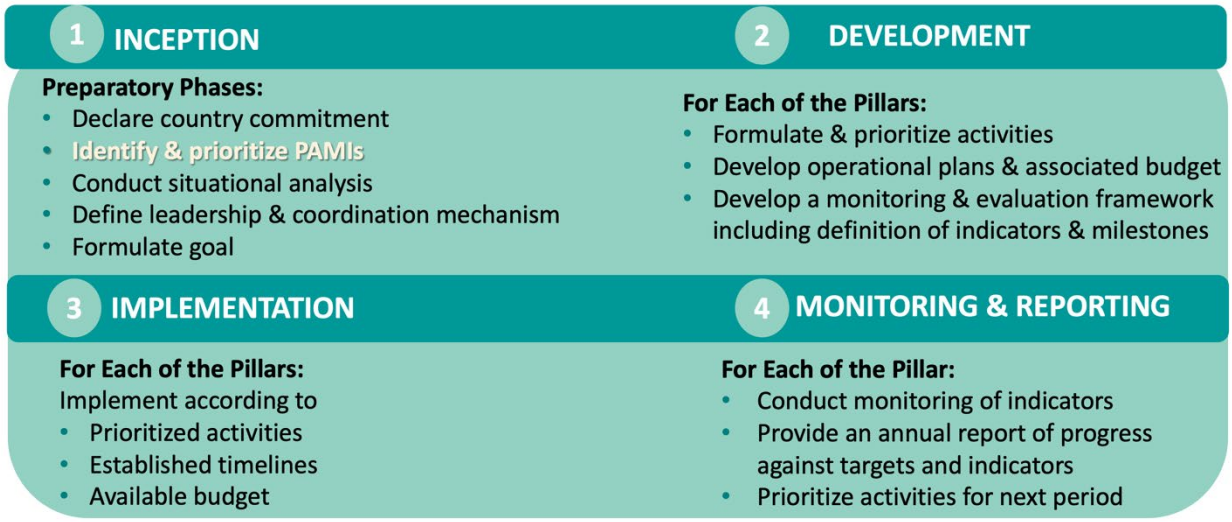
Moderator: ***Elizabeth Lee****, John Hopkins University*

Identification of priority areas for multisectoral interventions (PAMIs) and development of national cholera plans

D. Coulombier*, Country Support Platform (CSP)*

The importance of the identification of Priority Areas for Multisectoral Interventions (PAMIs) in cholera control and elimination is set out in the GTFCC Global Roadmap targets of a 90% reduction in cholera deaths and elimination of cholera in 20 countries by 2030, to be achieved using national cholera plans (NCPs) and spatially targeted multisectoral interventions that focus control and elimination programmes on specific, relatively small areas where the cholera burden is most concentrated, thereby maximizing public health impact and cost-effectiveness. These areas, previously known as "cholera hotspots," are "PAMIs" — priority areas for multisectoral interventions. The first step of the NCP process therefore includes the identification and prioritization of PAMIs (Figure 1) as a basis for activities implemented and monitored in steps 2-4.

Figure 1: National cholera plan (NCP) cycle



Not every PAMI needs to be prioritized for all pillars, and not every PAMI receives the same interventions. By nature, PAMI identification is a dynamic process that should be updated regularly.

To help implementation, the GTFCC is developing a range of tools to integrate PAMIs into cholera control.

GTFCC framework for the identification of PAMIs for cholera control

E. Lee*, John Hopkins University*

Dr Lee gave a précis of the development of the new PAMI framework. The previous method relied on incidence and persistence as metrics, but provided insufficient guidance on setting thresholds and taking additional factors into account. It was also inapplicable in countries reaching cholera elimination. Principles for the creation of the new approach were that it must be simple, generalizable, flexible and a tool that could facilitate long-term targeting and planning, while providing adaptability for use in different

transmission contexts. It does this by considering additional indicators (mortality, test positivity); providing harmonized scoring rules ; guiding selection of country-specific thresholds; emphasizing consensus-building among multisectoral stakeholders; and allowing selection of additional PAMIs based on vulnerability factors. It is also accompanied by a package of resources and tools.

PAMIs are recommended for use towards the beginning of NCP inception, with indicative advice to deploy the method in countries where cholera outbreaks have been reported in more than 5% of geographic units over the past five years. While previous (2019) guidance recommended to udate hotpot analysis annually, that has changed with a new focus on mid to long-term planning. PAMI updates are now recommended once every NCP development cycle.

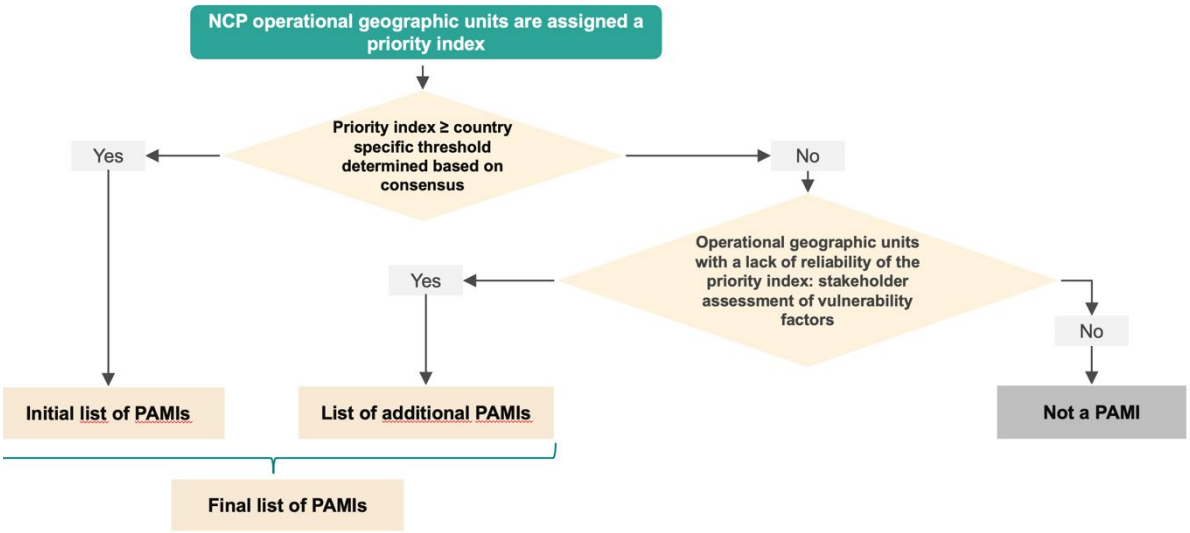
It should be noted that countries that have followed the 2019 guidance within the last five years should continue to follow their current plans.

PAMI identification is a three-step process of:

1. preparing datasets (defining the administrative level of the NCP operational unit and the analysis period, compiling surveillance and testing data and (optionally) supporting data on vulnerability; and performing quality control;
2. applying scoring according to a priority index (assessing and addressing missing data, scoring epidemiologic and test positivity indicators and calculating the priority index); and
3. validating stakeholders, building consensus and finalizing the list of PAMIs (holding workshops, validating data, writing a report on PAMI identification and planning NCP development in a participatory manner).

Selecting a priority index threshold value involves balancing the public health impact and achievement of national cholera control objectives with the feasibility of targeting all PAMIs with at least one intervention. Dr Lee talked through the data required to calculate the index and the approaches to assessing and addressing missing data; how to score epidemiological and test positivity indicators; and the calculation of the priority index. She ended by explaining the process of identifying the final list of PAMIs (Figure 2) and by highlighting the GTFCC-developed PAMI resources available at https://tinyurl.com/gtfcc-pamis (French versions were nearing completion at the time of the meeting).

Figure 2: Identifying the final list of PAMIs in a country



Discussion

- The epidemiological and testing indicators were chosen as the primary indicators in the belief that historical cholera burden is the most important predictor of future burden. In places with high to moderate transmission, there are likely to be too many places that require control measures, making it necessary to triage and prioritise the most affected. The vulnerability factors are used to supplement in places lacking good quality data.
- Guidance for countries with low to no recent transmission requires much more detailed description of vulnerability factors because it is impossible to rely on case data.
- There was discussion of where PAMI identification fits the wider planning and implementation of cholera control. After the PAMIs have been identified, there should be discussions about what to do in each one, mobilizing resources across pillars, targeting vaccination, WASH and other interventions, and triaging interventions. There is not much current guidance on this but this is being addressed in other working groups.
- Following the ideal trajectory of NCP planning, the number and distribution of PAMIs will decrease over subsequent rounds because interventions have been applied, until a country no longer meets the criteria for high to moderate transmission and can switch to the guidance for countries with low to no recent transmission. More robust and standardized surveillance will also enable better monitoring and evaluation.
- The term "operational geographic unit" is deliberately vague so as to give countries flexibility to choose the scale at which they perform analysis and at which their interventions and planning occur. In some countries this will be district level, where there is the strongest capacity for planning and operations; in others it might be at administrative level three. This will be determined by the scale at which a given country can plan.
- The testing indicators can use available tests. The basic data used for most of these indicators is suspected cases. Inclusion of all tests in the test positivity indicator is meant to strengthen testing surveillance as it becomes a more integrated, standardized part of prioritisation.
- Specific rules are applied to situations where data is missing depending on the type of missingness. Countries are encouraged to examine these closely rather than default to other methods like imputation of data.
- Consideration of local context is extremely important for the final selection of PAMIs, which places great emphasis on stakeholder validation and consultation with all the players in a given country.
- The first few countries to follow this guidance can be seen as an informal continuation of the pilot, and it is expected that the guidance will be further clarified over time based on national experiences.
- Not all interventions will be necessary in every PAMI. Rather, once the PAMIs are identified, they make up a set of locations on which to focus and establish which interventions to implement, where, and how.

Control case study: Identification of PAMIs in Bangladesh

***A. Rahman**, Bangladesh Ministry of Health*

Dr Rahman talked the meeting through the application of the new framework in Bangladesh based on data from a five-year period from 2018-2022. Applying the PAMI method in context, including the analysis of vulnerability factors related to severe weather events and climatic conditions, poor WASH coverage, population density and the special vulnerabilities of groups of refugees and asylum seekers, Bangladesh was able to plot new ways forward for its pre-existing NCP, which covers the period between 2019 and 2030. These included targeted improvements in national surveillance, including integration of rapid diagnostic test (RDT) test results and dehydration status and the enhancement of regional laboratories in

the PAMIs; creation of a common platform to integrate surveillance of water, waste water and diarrhoea; planning of multiyear PAMI- focussed OCV preventive campaigns; PAMI- focussed health awareness campaign in communities and schools and on traditional and social media before the peak cholera season; WASH inventions prioritized in PAMI areas. A first review of the PAMIs is planned in 2 to 3 years after implementation using the GTFCC template and integrating additional information on mortality and RDT results.

Lessons of this experience have included the importance of considering country-specify parameters and adapting chosen indicators according to the capabilities of the surveillance system; choosing relevant vulnerability factors in the same way; ensuring regular opportunities to discuss divisional results; using a tailored, modified template to present results and support discussion; and carrying out the planned 2-3 year review incorporating more information.

Prioritization of PAMIs for OCV use

***L. Breakwell**, US CDC*

The second axis of the GTFCC Roadmap is "…the use of a multisectoral approach to prevent cholera in hotspots in endemic countries, including using OCV as a bridge between emergency response and longer term control." Under the OCV preventive programme launched January 2023, countries need to develop multiyear plans of action (MYP) that document their OCV needs by year, based on PAMIs identified through the GTFCC tool, to inform vaccine forecasting.

Between January and April 2022, The OCV working group developed a tool to help countries do this, based on analysis of needs and country perspectives on prioritizing cholera hotspots for OCV, a deep dive into identified selection criteria, and discussion of thresholds and additional guidance for countries. This produced criteria in four categories –susceptibility, vulnerability, transmission risk and operations — further divided into mandatory, optional and operational criteria. Dr Breakwell talked through a couple of examples of how the tool should be applied, then explained how it had been designed to align and integrate with the PAMI identification criteria and tool. It is recommended that countries make maximum use of this alignment by completing OCV prioritization immediately after PAMI identification.

Piloting this approach in the Democratic Republic of Congo (DRC) as part of their MYP produced a few lessons, including some technical issues and a concern about how usable the tool would be by national cholera programme staff (the pilot was implemented by consultants). The next steps in refining the tool will be to update both the tool and the guidelines according to these findings; perform further pilots in Bangladesh, Cameroon and Kenya; and monitor scoring and prioritization. Once piloting is completed, the tool will be disseminated to countries and online to inform broader annual vaccine forecasting and allow better, more informative comparisons against demand scenarios.

Hands on PAMI tool workshop

***B. Sudre**, GTFCC Secretariat*

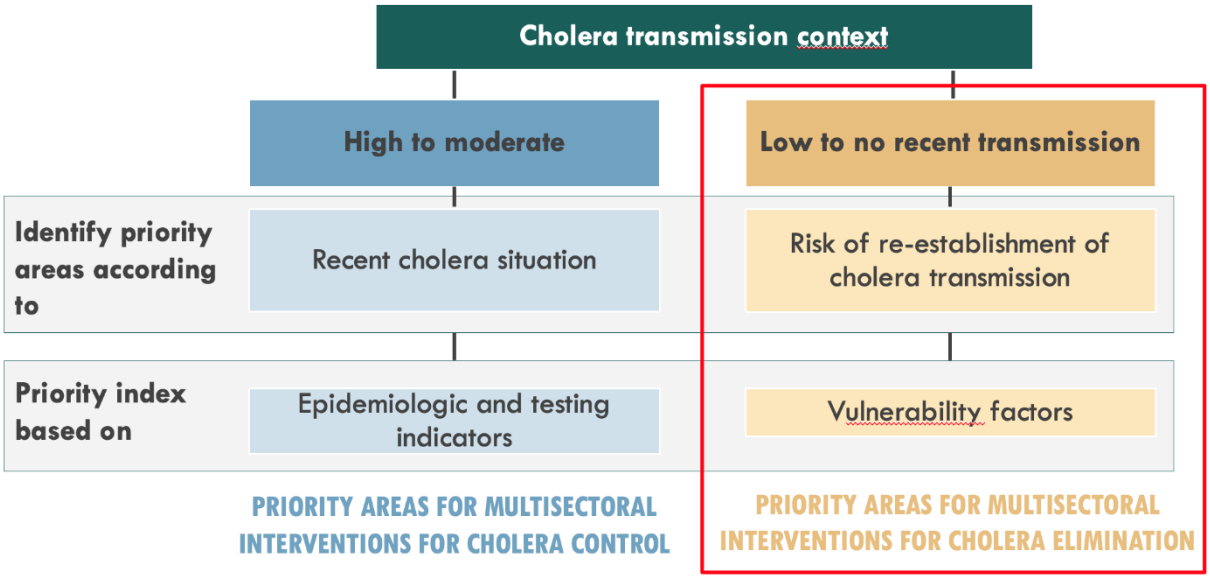
The session was followed by an optional workshop on the use of the PAMI identification tool, run by Dr B. Sudre of the GTFCC Secretariat.

GTFCC framework for the identification of PAMIs for cholera elimination

***E. Lee**, John Hopkins University*

The GTFCC guidance on using PAMIs for cholera control cannot be applied in an elimination context where very few cases would be reported in the analysis period (Figure 3).

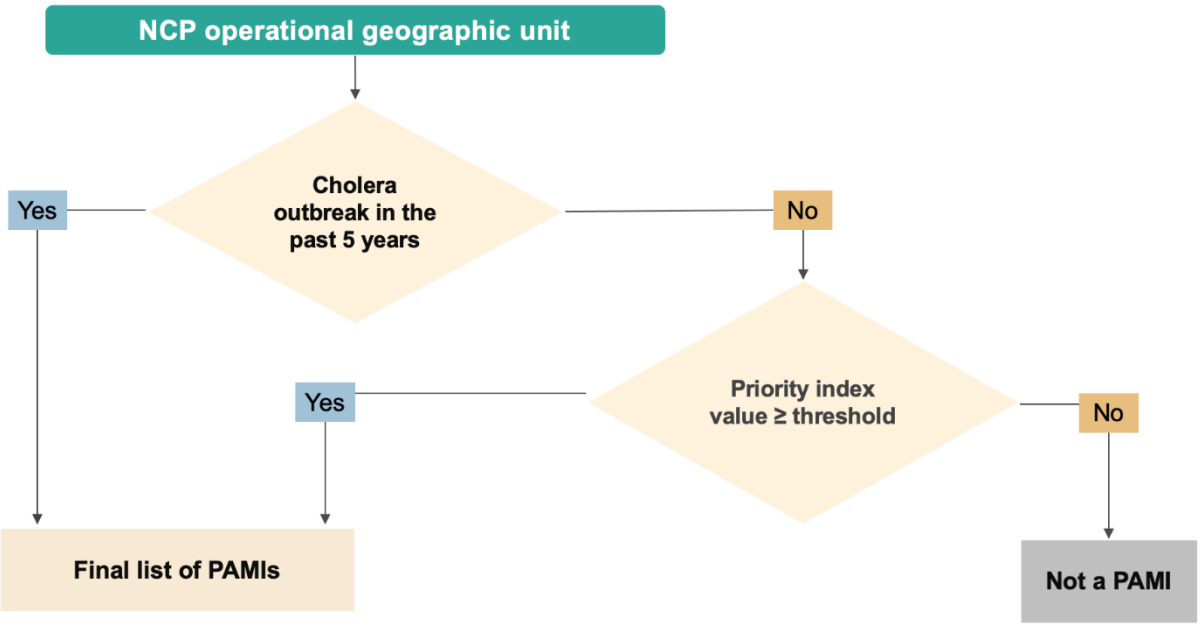
Figure 3: Cholera control vs cholera elimination in the PAMI framework



The GTFCC is therefore currently in the process of designing a method for using PAMIs for cholera elimination. This is intended for use towards the beginning of NCP planning in countries where cholera outbreaks have been reported in fewer than 5% of geographic units over at least the past five years. It again involves a three-step process of preparing datasets, priority index scoring and stakeholder validation, but with emphasized importance on vulnerability factors. Dr Lee presented an indicative list of vulnerability factors linked to at least one cholera outbreak phase (i.e. introduction, onset or spread) and split into WASH-related and non-WASH-related categories. Application of the WASH-related perspectives is based on standard definitions from the WHO/UNICEF Joint Monitoring Programme for Water Supply, Sanitation and Hygiene (JMP) and will depend on the data available in NCP operational units.

Under this system, once the vulnerability factors are scored, the priority index is created according to the sum of the vulnerability factor and WASH indicator scores and the selection of PAMIs carried out as per Figure 4.

Figure 4: Selection of PAMIs for cholera elimination



Once development of this approach is complete, an accompanying package of resources and tools will be created to help countries implement it.

Discussion

A period of discussion raised several points.

- If a country does not meet the criteria of cholera reports in fewer than 5% of units in the last five years, it should be following guidance for cholera control, not aiming for elimination. NCPs typically cover five-year periods, and the GTFCC position is that elimination is unlikely to be feasible in five years in a high to moderate transmission setting. Instead, a phased mechanism can be used to get to that point after one or two rounds of NCPs that prioritize control.
- Applying the tool without good WASH coverage or access data will require different approaches that are still under consideration. Some countries may have multiple sources of WASH data at different levels and resolutions; standardization may be difficult. The best approach in the short term may be to assume that higher level data applies to lower level operational units. The subgroup will work more on this.
- Places that have had large recent outbreak breaks, even after some time without cholera, should use the cholera control guidance– though the recommendation for that approach is to apply 5-15 years of data to the analysis, which will be impossible in countries with recent emergence or re-emergence.
- The GTFCC hopes that countries will provide as much insight as they can into how they adapt this tool to their own specific contexts.

Elimination case study: Identification of PAMIs in Mali

***J. Pomme**, WHO Mali*

Dr Pomme described the application of the new PAMI for elimination framework in Mali, a challenging context of simultaneous cholera outbreaks and re-emergence at the same time as a protracted humanitarian crisis and associated population movement. The tool was applied in the context of low incidence of cholera following a long inter-epidemic period (six years from 2014-2020). While Mali's national health system is fragile, there is national commitment to cholera elimination as per the Global Roadmap, and therefore a need for a method to identify at-risk districts in a context of low incidence.

The method was applied through a series of orientation and assessment meetings; data collection in the most affected areas; application of vulnerability assessment principles with a consensus-seeking approach; determination of vulnerability factors by submitting an indicative list for validation by national authorities; calculation of the global vulnerability index; then a series of data validation and elaboration workshops in two stages. The results showed elevated vulnerability in 21 health districts; intermediate vulnerability in 19; and low vulnerability in a further 35. These results were integrated into the NCP.

On evaluation the PAMI approach was found to have been beneficial in contributing to develop a national plan for cholera elimination, because it is a structured method that considers contextual factors. It allowed Mali to plan targeted interventions based on prioritization of the areas most vulnerable to reestablishment of community transmission.

Several limits to the approach were identified. Factors applicable to the tool as a whole included the fact that the framework is a simplified one based on general epidemiological knowledge, and therefore cannot incorporate all possible determinants of vulnerability, and the fact that it fails to consider the uncertainty of each factor. Country-specific limitations included the tool's inability to adapt to a large, multidimensional humanitarian crisis causing possible rapid change in some determinants; the limited availability of recent population data; and the fact that some data was missing at health district level and only available at higher administrative levels, making it challenging to compare health districts.

The Mali team offered solutions to these problems, including weighting vulnerability factors; creating a district vulnerability analysis plan; proposing different packages of interventions tailored to different by levels of vulnerability; and gathering and using the lessons and experiences of other pilot implementations.

Discussion: coordination and planning towards the Global Roadmap goals

***M. Martinez Valiente**, GTFCC Secretariat*

This session was intended to outline the current state of play concerning PAMIs and NCP development, but also to stimulate discussion on how to coordinate efforts and planning to achieve global roadmap targets.

The identification of PAMIs is the cornerstone of any work to achieve the ultimate targets of the Roadmap over the next 10 years. To do this, the global cholera community will have to orient and define joint activities to remove bottlenecks and improve responses to in-country challenges, including those that hinder PAMI identification.

M. Martinez Valiente outlined the countries that have identified priority areas over the past five years and those that have not. GTFCC target countries are identified in the Roadmap (though the current global situation may lead to the consideration and/or addition of further countries to the priority list). Approximately 48% of GTFCC target countries have done this work. Of these, 61% are in Africa, 43% in the Americas and 20% in Southeast Asia. These figures highlight both huge effort to date and great opportunities for further progress. There is work to be done to engage countries better in this exercise.

M. Martinez Valiente also presented an overview of NCP development to date. Eight countries have a finalized post-Roadmap NCP (Bangladesh, Ethiopia, Kenya, Sierra Leone, Somalia, Zambia, Zanzibar and Zimbabwe) and many more are engaged in developing or revising NCPs. Many have had plans in the past which, while they miss the criteria for a finalized NCP, represent significant work. Countries currently revising or developing NCPs include Burundi, Cameroon, DRC, Mali, Mozambique, Niger, Nigeria, Senegal, South Sudan, Sudan, Tanzania and Yemen. The past two years have seen a significant uptick in the number of countries with finalized or near-finalized NCPs. Of the 23 countries that have mapped their priority areas since 2018, 20 have developed or are currently developing an NCP.

There is a need to identify the next steps for the coming year, with the hope of generating and sharing planning perspectives for PAMI development. This requires insight into which countries plan PAMI identification or revision in the coming months, what their support needs may be, and what might prevent them from planning.

A period of discussion raised several points.

- Zimbabwe mapped hotspots some years ago, but the current outbreak there is driven by cases that are mostly outside those areas. This tool may not be of much use when a country's overwhelming priority is outbreak response.
- Many countries face financing and technical capacity shortfalls that hinder engagement with this process.
- Areas close to borders or which are shared with other countries face particular problems. There was some call for a platform through which countries managing cholera in cross-border areas can share information, particularly during outbreaks. The cholera community will have to improve information sharing to inform strategies, but this will be dependent on countries agreeing to share strategies (including with the GTFCC, which prefers to publish NCPs if permission can be secured). Cholera regional platforms can also be used for this purpose and have been established (in East and West Africa, for instance) to share documents related to NCPs, hotspot mapping, risk factors, action plans, etc., since before the Roadmap. The GTFCC has a role in disseminating this type of information, but leveraging other existing mechanisms is also important.
- The GTFCC needs to map countries planning to engage in the PAMI process, improve related information sharing processes, and coordinate relevant efforts and support.
- There was discussion of whether the GTFCC should establish a PAMI review process – for example, by establishing a group of experts to provide input into how well a country's PAMI efforts align with the GTFCC methodology.
- Kenya has done its mapping and has found each hotspot affected by different contextual factors. It would be useful to have guidance on how to identify contextual factors in each hotspot, select benchmarks against which to measure future progress, and target interventions based on context. Kenya would also welcome support in evaluating the impact of interventions.
- Cameroon is in the process of revising its NCP and working with WHO and other partners to integrate the results of a 2021 hotspot mapping into the plan. The country is facing outbreaks all over its territory and at the time of the meeting had over 15 000 cases, making it difficult or impossible to discuss elimination. Competing priorities are to some extent overwhelming, making it impossible to follow through longer term elimination activities.
- The GTFCC is aware of gaps in the guidance on how to identify and prioritize activities to be implemented in PAMIs. This will be addressed.

Conclusions and wrap up – action items for the GTFCC Working Group

*Moderator: **E. Lee**, John Hopkins University*

Dr Lee wrapped up the day with a summary of action items for the subgroup. She expressed these as follows:

- Translate the PAMI guidance into French and any other necessary languages
- Continue developing and piloting PAMI elimination guidance
- Clarify how WASH indicators and other factors can best be integrated into the process
- Think more about integration of the PAMI activities with intervention support activities
- Clarify how PAMIs feed into OCV prioritization
- Reflect on how to clarify usage of these tools, including through improved guidance for countries that fall between the control and elimination criteria (e.g. those facing reemergence after several years of interrupted transmission)
- Follow up with countries starting to implement PAMI control guidance and solicit more feedback on needs for additional materials (e.g. job aids, infographics, video tutorials etc.) to support the use of the tools
- Follow up with smaller group discussions to understand the potential utility of a PAMI review process to facilitate coordination and technical support.

Cholera surveillance at country level

Moderator: ***K. Heitzinger****, US CDC*

GTFCC recommendations for country surveillance

K. Heitzinger*, US CDC*

Dr Heitzinger began this session by presenting the 2023 GTFCC Interim Recommendations for Cholera Surveillance and soliciting feedback to be considered before the next update.

Cholera surveillance is the cornerstone of the GTFCC Roadmap and a critical requirement for all other pillars, allowing early detection and quick responses to contain outbreaks; targeting of prevention strategies and identification of PAMIs; and high quality monitoring and evaluation (M&E). Because the older (2017) recommendations have proved not to provide an adequately detailed or accurate picture of cholera, or to address adequately the diversity of epidemiological situations and corresponding surveillance and control objectives, the GTFCC undertook to update the recommendations.

The key objectives and principles of the revision, as set by the working group in April 2022, are to maximize the operational use of cholera surveillance data through adaptive surveillance at the local level; to increase the accuracy of cholera surveillance through systematic testing strategies; and to increase the resolution of cholera surveillance through case-based surveillance. This approach incorporates the following new definitions:

- **Suspected cholera outbreak**: Two or more suspected cholera cases reported in the same surveillance unit within one week of each other; **or** one person ≥ 2yrs old 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**: A probable outbreak is detected when a certain number of suspected cholera cases with a positive rapid diagnostic test within a two-week period in a surveillance unit exceeds pre-defined thresholds
- **Confirmed cholera outbreak**: At least one confirmed cholera case locally acquired (an imported cholera case is not a confirmed cholera outbreak)
- **End of a cholera outbreak**: 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.

Adaptive cholera surveillance must be both stable and flexible. Regardless of the cholera situation, surveillance should include health facility-, community- and event-based operational surveillance streams, systematic data collection and reporting, and routine data analysis of key indicators. Surveillance modalities should be adapted to the prevailing cholera situation as reflected by the surveillance unit's choice of case definitions, testing strategy and frequency of reporting and analysis. A summary of the adaptive approaches can be seen in Figure 5.

Figure 5: Core vs adaptive surveillance approaches

Cholera situation in the surveillance unit	Absence of confirmed cholera outbreak	Confirmed cholera outbreak
CORE MODALITIES	DETECTION	
	Systematic case detection through all surveillance streams (health-facility, CBS, EBS)	
	DATA COLLECTION	
	Routine recording and reporting of minimum case-based data	
	ANALYSIS	
	Systematic data analysis at the surveillance unit level	
ADAPTIVE MODALITIES	CASE DEFINITION	
	Suspected and confirmed case definitions in surveillance units where there is no confirmed outbreak	Suspected and confirmed case definitions in surveillance units where a confirmed outbreak
	TESTING STRATEGY	
	Testing of all suspected cases	Testing of a subset of suspected cases according to a systematic protocol
	FREQUENCY OF REPORTING AND ANALYSIS	
	Daily	At least weekly

In the next phase, these interim recommendations will be enriched by further differentiation of cholera outbreak situations in a surveillance unit, including their articulation with the requirements for cholera-free status; identification of deteriorated transmission situations, as a trigger for further investigation and stepped up in response and control efforts; additional guidance and practical tools for data collection, reporting and analysis; recommendations for monitoring and evaluation of surveillance performance; and incorporation of country feedback.

GTFCC Interim cholera-free status framework

***K. Heitzinger**, US CDC*

Dr Heitzinger presented the GTFCC interim framework for the recognition and maintenance of national cholera-free status. The Roadmap targets elimination of cholera as a threat to public health in 20 countries by 2030, as defined by absence of community transmission of cholera documented for at least three consecutive years based on a well-functioning epidemiologic and laboratory surveillance system able to detect and confirm cases.

The framework was developed to provide a harmonized, transparent basis for GTFCC target countries and regions to document their achievement and maintenance of elimination of cholera disease as a threat to public health, and for the GTFCC to be able independently to assess, recognize, and monitor progress towards elimination. The interim framework was presented at the meeting to sensitize potential pilot countries (emphasizing its flexibility and the scope for further change) and recap key piloting requirements so that potential pilot countries could come forward.

The requirements for recognition of cholera-free status are absence of community transmission and appropriate and well-performing epidemiologic and laboratory surveillance. The requirements for maintenance of recognized cholera-free status are continued absence of sustained or widespread community transmission; tolerance for limited community transmission; and presence of appropriate and well-performing epidemiologic and laboratory surveillance. Procedurally speaking, a country would submit standard dossiers to the GTFCC for initial recognition, annual maintenance and/or re-

establishment after any suspension that might occur. These would be reviewed by a GTFCC cholera-free-status Independent Review Panel, which would then make a decision.

In conclusion, cholera-free status does not have to mean absence of any cholera cases – provided transmission in the community is prevented and countries document compliance with applicable requirements – but a recognized status is subject to maintenance and can be suspended. The Panel's assessment is independent and transparent.

Hearing from countries

Moderators: **P. Okitayemba**, DRC; **J.P. Langa**, Mozambique

The group was taken through the results of a pre-meeting survey that gave a rough picture of the state of cholera surveillance at country level. As well as reporting and discussing these results, the aim of this session was to examine perspectives for implementing the GTFCC surveillance recommendations and identify action items for the Working Group.

100% of the 25 countries surveyed implemented health facility-based surveillance; 72% had community-based surveillance (CBS); 72% implemented event-based surveillance (EBS); and 64% of countries implemented all three.

Case-based data was reported in health facilities in 76% of countries and at national level in 68%, with some countries using both systems simultaneously; and zero reporting was undertaken in 86% of respondent countries.

Epidemiological data was handled electronically in 16% of countries, on paper in 4%, and through a mix of the two in 80%. For lab data these figures were 40%, 12% and 48% respectively.

For electronic reporting, DHIS2 was the most frequently used tool (in 12 countries). Other tools included ad hoc online systems, Excel/Google spreadsheets, Epi Info and IDSR.

The lowest level of integration of epidemiological and laboratory data was national level in 42% of countries; administrative level 1 (e.g. provinces) in 16%; and administrative level 2 (e.g. districts) in 42%.

The lowest level of availability of sitreps/epidemiological bulletins was national in 42% of countries; administrative level 1 in 25%; administrative level 2 in 21%; and administrative level 3 (e.g. counties) in 12%.

As the results of the survey were presented, participants at the meeting were given opportunities to discuss the results in light of their own experiences of surveillance. This enabled participants to hear about descriptions of the approaches to cholera surveillance taken in Togo, Zimbabwe, DRC, Cameroon, Afghanistan, Somalia, Haiti, Lebanon, Zambia, Nigeria, Uganda, Niger, Mozambique and Kenya.

Conclusions and wrap up – action items for the GTFCC working group

***K. Heitzinger**, US CDC*

Dr Heitzinger wrapped up the session with a summary of the action items for the subgroup. She expressed these as follows:

- Continue developing the comprehensive surveillance recommendations, taking into account the feedback from this meeting and any subsequent inputs
- Consider gathering in-country experiences of these recommendations to analyse their added value and areas for improvement
- Consider developing additional materials, tools or resources to help operationalize these recommendations

- Move forward with adjustments to the cholera-free status framework based on changes to the interim recommendations and development of the comprehensive recommendations
- Pilot the cholera-free status framework.

Cholera surveillance at regional and global levels

Moderator: ***A. Medley,*** *US CDC*

Global overview of the cholera situation

N. Fischer*, WHO Cholera Technical Team*

Dr Fischer provided a brief overview of cholera around the world at the time of the meeting. 25 countries in five WHO regions had reported cholera outbreaks at that point in 2023.

In South East Africa, Malawi was experiencing the largest active cholera outbreak in Africa, with 58 415 cases and 1 755 deaths for a case fatality rate (CFR) of 3.0% as of 1st May 2023, but a decreasing trend in cases since the end of January 2023. Mozambique had been suffering a widespread outbreak since September 2022, with 29 280 cases and 131 deaths (CFR: 0.4%) as of 30 Apr 2023. Zimbabwe had been experiencing a fast-growing outbreak since February 2023, with 718 cases (125 confirmed) and 18 deaths (CFR: 3.0%) as of 30th April 2023.

In the Horn of Africa, an outbreak was ongoing in the "Mandera Triangle" where the borders of Kenya, Ethiopia and Somalia meet and population movement exacerbates cross-border transmission. The Kenyan outbreak had seen 9 838 cases and 157 deaths (CFR: 1.6%) since October 22, with data up to 30 April 2023; Ethiopia had had 5 525 cases and 84 deaths (CFR: 1.5%) since August 2022, as of 1 May 2023; and Somalia had seen 6 305 cases and 19 deaths (CFR: 0.3%) since January 2023, as of 23 April 2023.

In Central Africa, Cameroon had a large outbreak in 2022, with over 15 000 cases. 2023 had seen 854 cases and 38 deaths (CFR 4.4%) as of 30 April 2023.

In the Middle East, an outbreak in North West Syria had seen a total of 67 310 suspected cases and 23 deaths, with a CFR of less than 1%, between September 2022 and April 2023. Around 19% of these cases were in camps housing internally displaced people (IDP) and 45% of cases were in children under 5 years old.

In Hispaniola, an outbreak in Haiti had had 40 678 cumulative cases (2592 confirmed) and 650 deaths, a CFR of 1.6%; and the Dominican Republic had reported 99 confirmed cases and 0 deaths, with 75% of cases in the capital city of Santo Domingo.

In South East Asia, Bangladesh had reported 99 cases (70 confirmed) with no deaths.

Regional and global cholera surveillance – why does it matter?

A. Medley, *US CDC*

The scope of the regional and global surveillance GTFCC sub-working group has historically been to support cholera preparedness and outbreak response and monitor progress along the Roadmap. A recent landscape analysis found a lack of uniformity and differing levels of engagement across various surveillance and coordination activities, causing the group to consider what core objectives and principles for regional surveillance could look like — but this work was hampered by the 2023 cholera situation and

major shifts in the global cholera landscape. The subgroup is now examining what has worked in this space, what gaps exist, and what possible solutions could strengthen regional and global surveillance and the ways in which it supports national and regional preparedness and response—noting that "cholera surveillance in countries within a region" is not the same as regional cholera surveillance.

The landscape analysis identified three main priorities, or goals:

- To develop, animate and sustain strong cholera networks (timely and robust alert or reporting channels) across borders, regionally, and globally
- To collect, validate, analyse, interpret, and disseminate data on the cholera epidemiological situation and risk of spread at the regional and global levels, to foster coordinated regional preparedness and response
- To monitor and support countries to strengthen cholera surveillance by assessing their modalities and performance for cholera surveillance.

To support these goals, regional and global surveillance should have three main attributes:

- it should be a low burden activity, to encourage country participation;
- Outputs should be timely, fit for purpose, and informative to stakeholders; and
- participation should ultimately strengthen country surveillance.

Regional and global cholera surveillance – where do we stand?

WHO Headquarters

C. Schultz, *WHO Geneva*

In service of global cholera surveillance, WHO is working in two main areas: developing a global cholera database and developing cholera analytical outputs.

The database consolidates cholera data from different regions to build a global dataset, harmonize data across regions, and offer a central source of data for global and regional reports. The analytical outputs that WHO offers include week-to-week epidemiological updates; epi curves; attack rate maps; and severity and forecasting data. These are available from district to regional level and allow the identification of trends, geographical spread and areas with risk for cross-border transmission. Dr Schultz explained how this data is collected, entered, stored, cleaned, analysed and turned into outputs, then listed the achievements that have resulted from these efforts. These include products from WHO headquarters such as the weekly global cholera data pack and a monthly global cholera sitrep; support to the Regional Office for Africa in producing its weekly regional cholera data pack and bulletin and the daily cholera reports; collaborative work with regional and country offices, including deployments and provision of remote training sessions; and relationship building to strengthen cholera collaboration between headquarters and regional and country offices.

There have been challenges. Data collection has been hampered by a lack of uniformity in national sitreps; incompleteness; reporting delays; retrospective corrections; and difficulties with data collection in the field. Data sharing has been hampered by bottlenecks between ministries of health and WHO country and regional offices, and poor data sharing at provincial and national country levels that affects larger scale work. Finally, data entry has suffered due to human resource limitations that have made continuous manual extraction of data from sitreps unsustainable.

The next steps will be to increase engagement with country offices, ensuring smoother flow of data between ministries and the three levels of WHO, working towards consistent daily and weekly data and a shift in effort from data entry to analysis; to develop version 2 of the global data entry template to ensure

harmonized reporting consistent with GTFCC recommendations; to automate data flows to generate fast outputs and facilitate creation of data packs, daily reports and weekly bulletins in countries, regionally and globally; and to set up the global cholera dashboard.

Africa regional situation update

***F. Sanni**, WHO Regional Office for Africa*

Cholera in the African region tends to happen in challenging contexts variously affected by natural disasters, conflict, cross-border movement, multiple other disease outbreaks, strained resources, shortages of medical commodities including cholera kits and OCV, and unreliable WASH. On average, 12 African countries report cholera cases annually.

In 2018 African Member States adopted the Regional Framework for the Implementation of the Global Strategy for Cholera Prevention and Control 2018–2030, which defines clear milestones for regional cholera elimination; but with current cholera outbreaks Africa is off track in its work to achieve the Roadmap goals. The continent saw an exponential rise in cholera cases in 2023, and from 2014-2021 accounted for 21% of reported cholera cases and 80% of deaths globally. In January 2023 new cases rose by almost 30% of the 2022 total and the cumulative number of cases at the time of the meeting had risen to around 60% of the 2021 total.

Cholera surveillance across the continent varies by country, but generally involves a combination of active and passive surveillance methods in communities and health facilities, and event-based surveillance. There is continuous work to build capacity of staff and rapid response teams have been established to investigate cases and conduct contact tracing. Surveillance officers and data analysts are deployed in high-burden countries to improve reporting and data quality, and a range of surveillance tools has been disseminated, including a Weekly Aggregate Reporting Tool and a line-listing form. WHO supports countries to strengthen cross-border surveillance.

The WHO Regional Office for Africa depends heavily on daily data scraping from sitreps, with other data sources including line lists, weekly presentations, bulletins and aggregated tools, and IDSR. Outcomes are shared through daily cholera updates and weekly regional updates, bulletins and media talking points.

The regional office works on cholera in collaboration with other stakeholders including district and local traditional leaders, village health committees, frontline health and extension workers, ministries of health and other multilateral partners including UNICEF, the Africa Centres for Disease Control and Prevention (Africa CDC) and the US Agency for International Development (USAID). Together they face a range of challenges across the continent including delayed and insufficient data sharing, weak surveillance, poor cross-border surveillance along porous borders, competing priorities and limited resources, inadequate training, limited WASH, poor access to health services, environmental issues impacting water safety, and – currently – unprecedented outbreaks overwhelming healthcare systems.

The next steps in facing these challenges will be to enhance surveillance across all affected areas; continue mobilizing resources for cholera readiness and response; regular coordination and operational meetings for strategic planning with affected countries; continued strengthening of cross-border collaboration on cholera surveillance; intensified risk communication and community engagement through media and local leaders; helping activate national cholera task forces in impacted countries; providing WHO support for lab commodities in affected regions; providing case management training for outbreaks; deploying technical experts to support responses; and providing technical support to vaccination strategies for reactive OCV campaigns.

Cholera surveillance in the Eastern Mediterranean – a regional approach

***S. Elnossery**, WHO Regional Office for the Eastern Mediterranean*

More than 76 million people in the Eastern Mediterranean Region are directly or indirectly affected by political conflict, environmental threats and natural disasters. The region has the largest population of displaced people of any WHO region, including 17.1 million IDP and 16.7 million refugees, all of whom face limited access to basic health care services and environmental health infrastructure; eight of the world's most challenging complex humanitarian emergencies are in the Eastern Mediterranean. Cholera remains a major public health risk.

At least 13 of the 22 countries in the region have reported cases in the last decade. It is estimated that 188 000 cholera cases occur annually in the region, but accurate quantification is limited due to weak surveillance (though all 22 countries categorize cholera as "immediately reportable" as part of routine surveillance). Eight countries reported acute watery diarrhoea (AWD)/ cholera cases during 2022, most of which are facing emergencies and reporting through the EWARN system. Other countries in the region report very few numbers, most of which are categorized as imported cases.

Surveillance varies according to country. In more stable nations reporting is case-based. EWARN is implemented in eight countries plus certain specific affected districts of Pakistan. Data is collected at subnational level from sentinel sites, and aggregated data is collected by sex and age. Some countries, such as Somalia, use additional platforms to collect cholera data, such as the Cholera Outbreak Portal. Confirmation is done through RDTs on stool samples from every 10th patient meeting the case definition, with cultures on 10% of positive RDTs. Sample collection, transport and testing are affected by accessibility and security conditions and availability of resources, supplies and reagents.

Case-based data or line lists are shared with the WHO regional office on an ad hoc basis during outbreaks, and aggregated data and situation reports are more forthcoming. Somalia regularly shares weekly cholera sitreps and the EWARN weekly bulletin, and Pakistan, Afghanistan and Syria share weekly bulletins. Data sharing was better in several countries before 2021, but during outbreaks countries tend to share more. The regional office produced a weekly sitrep and monthly bulletin for Somalia and Yemen, but this also stopped in 2021. A Regional Cholera Platform is being developed to serve mainly as a repository for guidelines, reports and donor alerts. To date regional data has mainly been used for planning, monitoring the regional cholera situation, monitoring preparedness and prevention programmes and activities, and supporting national cholera policies and planning.

The regional office collaborates with a range of stakeholders and partners to lead cholera prevention, detection and response, serving as the central body for regional technical and emergency support for cholera. The exact roles of regional partnerships in collecting and using regional data are still not well defined.

Challenges across the region include a very high risk of spread, including to refugees, IDPs and illegal migrants; continued conflict, economic crisis and population displacement; difficulties coordinating with multiple hubs and authorities; extreme weather; and poor transparency and information sharing from governments. This last issue creates particular challenges for a regional data approach: cholera data is not regularly shared, outbreaks are not always officially declared due to fear of economic losses, and countries are widely uninterested in establishing and/or strengthening the cholera surveillance system.

In summary, the main challenges are weak surveillance systems; underreporting due to political pressure; lack of laboratory capacity in some countries; lack of stakeholder coordination; limited preparedness for seasonal outbreaks; reactive responses after epidemics; limited resources for the public health control; and a lack of cross border collaboration between neighbouring countries. In addition, there is an absence of active laboratory-based surveillance for epidemic diarrheal diseases in general; there are no emergency stockpiles of drugs and other supplies; water is often unsafe at point of use (partly due to absence of effective treatment strategies for portable water, including storage); there is an unmet need for social

mobilization campaigns and risk communication; and the situation as a whole is exacerbated by critical knowledge gaps. Urgent investment is needed to prevent outbreaks, with a particularly critical unmet regional need for WASH.

The regional office sees a way forward based on five pillars:

- **Leadership and coordination**: enhancing national and subnational multisectoral coordination and documenting best practices and knowledge gaps
- **WASH**: Investing in WASH infrastructure
- **Strengthening core response capacities** for health, particularly in early warning surveillance and laboratory diagnosis, case management and infection control
- **Risk communication and community engagement** (RCCE) to enhance cholera prevention knowledge in the public and among frontline health workers
- **Vaccination**: timely introduction of OCV.

WHO Regional Office for Southeast Asia

P. Murthy, *WHO India Country office on behalf of the WHO Regional Office for South-East Asia*

Cholera is not only endemic in the Southeast Asian Region, but also underreported and underestimated. Recent years have seen an increasing number of outbreaks, and cholera is often introduced to other continents from Southeast Asia. The region has an estimated 500 000–700 000 cholera cases (often labelled AWD but not officially reported) and 10–30% of diarrhoea cases in Bangladesh and India (as detected by systematic hospital-based surveillance) are due to cholera. A substantial proportion of cases are missed because of inadequate stool culture. Bangladesh estimates 450 000 cholera cases are hospitalized each year, 4 500 of whom will die.

Focussing on the three Member States in the region for which cholera is a priority — Bangladesh, India and Nepal — existing surveillance objectives and modalities are designed for early warning and response, monitoring trends, estimating burdens, and monitoring the impact of interventions. Suspected cases are routinely detected via health facility-based surveillance, EBS and CBS. Verification and RDT positives are reported within 24 hours and suspected cases are reported weekly as AWD/Acute Gastro Enteritis. Data collection, reporting and interpretation are done electronically and routine data is interpreted mostly at provincial and national levels. Surveillance outcomes are disseminated through dashboards, disease bulletins and annual surveillance both publicly and through some restricted-access forums, and contain information on early warning and response, trends, burdens and hotspots. This is used to support evidence for preparedness and response reviews and planning policy and programmes.

For regional cholera surveillance, the regional office works with country offices to monitor outbreaks and collect related data. Regional data is published weekly for internal use (with a switch to external publication planned), and an annual cholera report is published in the Weekly Epidemiological Record. A regional WHO Collaborating Centre in Kolkata compiles the regional burden based on published reports and Indian data. Stakeholders include municipal agencies and departments of public health engineering; ministries of the environment; actors in the WASH sector and other partners; and academia, research institutions and WHO Collaborating Centres. Regional achievements to date have included sustained sentinel surveillance; early outbreak alerts; regular reporting of AWD and cholera; enhancements of rapid response and outbreak investigation capacity through trainings; use of surveillance data and outcomes to inform policy and programmes; and informed recognition of cholera as a priority for the region, reflected in a regional diagnostic and genomic sequencing roadmap.

Challenges to this work include underreporting (only lab-confirmed cholera cases are reported, while suspected cholera among AWD cases is recorded but not reported; EWARS and EBS, including CBS, need

strengthening; and transparency can be affected by economic, social and political disincentives); poor laboratory capacity for confirmation, especially subnationally, making it hard to estimate the proportion of AWD cases that may be due to cholera; limited subnational data analysis and interpretation capacity; poor multisectoral coordination (coordination around WASH is particularly limited); restricted human and financial resources, including to sustain surveillance sites; frequent staff turnover; and a preponderance of federal structures characterized by variable subnational capacity and implementation.

Cholera in Hispaniola: Haiti & Dominican Republic

***J.M. Gabastou**, WHO Regional Office for the Americas*

Haiti suffered an horrific cholera epidemic in 2010, with 820 000 cases leading to 9 792 reported deaths. In February 2022 the country marked three years without a documented cholera case, but in September of that year a new outbreak began in Port-au-Prince. In the Dominican Republic, a first imported cholera case was confirmed in October 2022.

Cholera control in Hispaniola follows an integrated approach, with work to control morbidity and mortality by supporting the ministries of health and partners with case detection and investigation and case management. Diagnosis, surveillance and treatment guidelines have been updated, and work has been done to reduce spread and protect vulnerable groups through targeted risk communication and OCV (Haiti has administered 850 067 doses with 76% coverage and the Dominican Republic has administered 53 205 doses targeted to health care workers and neighbourhood contacts). Interinstitutional and intersectoral coordination has been strengthened to ensure adequate WASH in affected provinces. The ministries of health have been supported through a wider regional programme to prepare and improve readiness for investigation, detection, confirmation, and early response to cholera alerts, and regional virtual training has been provided for laboratory diagnosis and molecular characterization of V. cholerae based on updated WHO guidelines. Essential supplies have been purchased and stocked in Panama, and genomic sequencing is implemented in Haiti. Hispaniola sitreps and alerts are shared weekly through a PAHO dashboard. In all this the regional office is working and/or coordinating with stakeholders and partners including US CDC, the Public Health National Laboratory of Haiti (LNSP), the IFRC, UNICEF, the UN Humanitarian Air Service, and many more.

Outcomes and achievements to date have included training laboratory personnel and equipping labs across Central America and the Caribbean for early diagnosis and confirmation of V. cholerae. Personnel have been certified for transport of infectious substances. The mobile “labo moto” lab service in Haiti has been reactivated and sentinel sites have been activated for alert and early response across the island. Active community case investigation and neighbourhoods contact tracing are in place. Missions to evaluate the quality of case management in cholera treatment centres (CTC) are ongoing. Risk Communication materials have been developed in French, Spanish and Creole. Haiti has engaged with the International Coordinating Group on Vaccine Provision (ICG) to request permission to use remaining OCV doses to vaccinate prison inmates. In Haiti, PAHO/WHO also leads the coordination of a Health Sector Group that includes other UN agencies, NGOs and the donor community.

Challenges to this work in Haiti include a complex humanitarian and socio-political crisis causing high levels of insecurity, fuel shortages and economic instability, all of which continue to impact response capacity by hindering activities such as the transport of patients to CTCs; health promotion; efforts to increase community-level access to health and basic WASH services, food and water; epidemiological surveillance; installation of oral rehydration points (ORP) and CTCs; and distribution of life-saving cholera medicines and supplies. This is exacerbated by a lack of qualified health care workers and epidemiologists and high demand for medical and non-medical supplies, including OCV, that limits the amount of cholera commodities available for distribution.

In the Dominican Republic, cholera response is affected by limited access to WASH services and safe water across most of the country; limited follow-up on epidemiological surveillance in border provinces; and political unrest around local and national elections.

Discussion: Regional and global cholera surveillance – the way forward

A. Medley, *US CDC;* ***P. Barboza,*** *GTFCC Secretariat, WHO Cholera Technical Team*

This discussion covered a range of topics, including perceptions of regional and global surveillance, incentives to participate, the effect of suboptimal regional/global surveillance, obstacles to data sharing, solutions to barriers, and country needs. Many of these points will be taken forward by the working group.

- Recording and reporting cases that visit oral rehydration points (ORPs) is a challenge. Health workers at ORPs may not be able to use case definitions well, and it is possible that there is a lot of under-reporting of cases that end up at ORPs then go home.
- Leveraging existing systems will be important in countries struggling with resources, taking an integrated approach where possible and linking community-based surveillance with existing systems. From an implementation perspective, most of the people carrying out cholera surveillance are the same who would carry out surveillance for other diseases, applying lessons from one disease to another. The working group has taken care not to develop cholera guidance in a siloed manner, locating it in the context of existing other systems. Integrated surveillance systems in countries that can record multiple diseases will lighten the workload for all.
- The GTFCC needs a strategy for cross border surveillance, which has been identified as a weak point. In many places, particularly in southern Africa, countries are seriously affected by cholera events in neighbouring states. Biweekly country meetings are held in the Africa region, one with Francophone countries and one with Anglophone countries, as a first step towards cross border information exchange. These involve structured requests to countries for specific slide decks on their cholera situation, key challenges, and requests for WHO action.
- The recommendation for the increased collaboration and information sharing necessary for better cross border surveillance often comes at high level meetings rather than at programme level, where more communication is needed, especially around borders. It can also be complicated by protocol issues, SOPs, issues of foreign affairs, etc. In the past, networks have existed for this purpose – the African Cholera Network, for example, or the UNICEF-supported Southern Africa Cholera Surveillance Network – and these could be resuscitated.
- However, there are serious issues around the confidentiality or ownership rules needed for data sharing. It would be good to know countries' boundaries and minimum requirements around data security.
- WHO headquarters prepares a weekly cholera data pack which is shared internally with regional offices, and slide packs that are shared under confidentiality disclaimers with GOARN members. WHO has also prepared a first global public situation report and is in the process of preparing the second. The data sharing approach for this project was to verify what information was already available in the public domain, and then to reach out to country offices and check what could be included for specific analyses.
- Line lists present more issues and cannot easily be used on public platforms. WHO has no specific framework or bilateral data sharing agreements and so for now operates within the WHO network only, or with verbal or written agreements with countries.
- Gavi is hoping to launch an application window this summer for countries to request cholera RDTs, and hopefully molecular tests as well next year. Gavi needs information that shows how the vaccines or tests it procures are being used, and how distribution is working. The type of data being requested around cholera – numbers of suspected cases, how many are tested, with what and with what results – is exactly that. Gavi is therefore hoping to tie diagnostic procurement support to country reporting to WHO on use of the tests. In some contexts, therefore, it may be in countries' interests to provide data to a single point, like WHO, from where it can be shared onward where necessary.

- WHO has been working on data sharing for some years and has experienced several barriers. To be able to share information, information must be coming in, which is not always the case. For years WHO has had to extract data from sources (such as PDF files and sitreps) that make it difficult and challenging to do anything meaningful with it. What can be done with this data is also limited by resources: a cholera data platform analogous to those in place for influenza and meningitis would need to be sustained, and partnership will be crucial to doing that.
- If more information is received, more can be shared back, as long as the data is of sufficient quality. Progress is being made to encourage countries to share, and more and more are doing so, but this is work in progress. To encourage sharing, the benefits should be more visible.
- It would be useful to hear from countries about the barriers, and the minimal requirements and standards that would have to be met for them to share surveillance data more openly. It would also be good to have suggestions as to who should be able to receive that data — whether that be WHO regional offices, WHO headquarters, or regional actors like cholera platforms. Feedback from country representatives in the room revealed several issues. Historically data has tended to be shared with partners through IHR focal points and through weekly bulletins or sitreps. Better guidance is needed. Other challenges in countries include timely reporting and notification, the many different reporting channels, and the complexity that sharing can add to already strained processes.

Conclusions

P. Barboza, *GTFCC Secretariat, WHO Cholera Technical Team*

Even in 2023, a significant proportion of the signals received about cholera outbreaks around the world come through event-based surveillance. New and improved systems are needed through which everybody can access the information they need while ensuring the necessary levels of privacy and data protection.

Information should be shared at the same time across ministries, WHO country and regional offices and headquarters. Data – which should not contain names – should be easy to import to a central platform from DHIS2 and other systems. Achieving such an objective will not be easy: it will require sustainable resources to develop, and more resources, including staff, to perform meaningful analysis.

Not all countries are in the same place: this will be easy to achieve for some Member States and more complicated for others; but any step in the right direction brings us all closer to elimination.

When data is collected and shared for so many other diseases, there is no reason that it cannot be done with cholera. Despite all the difficulties, it is a necessary goal: fighting cholera and cholera advocacy will be far easier with an accurate, up to date cholera map. This is not information for the sake of information, but information for action.

The session closed with an acknowledgement of the great work over the last three years of the outgoing Chair of the regional surveillance subgroup, Alexandra Medley.

Testing and confirmation of cholera

Moderator: ***M.L. Quilici,*** *Institut Pasteur Paris*

GTFCC interim testing strategy

K. Heitzinger, *US CDC;* ***M.L. Quilici,*** *Institut Pasteur Paris*

The GTFCC testing recommendations are being revised in the context of a recent upsurge in outbreaks and the observed challenges and limitations of surveillance (including low testing rates, irregular testing, and lack of integration of epidemiological and laboratory data). The February 2023 provisional update of the GTFCC Interim guidance on public health surveillance for cholera supersedes the 2017 guidance and aims to ensure that surveillance data provides an accurate, sufficiently granular epidemiological picture and more up-to-date testing recommendations.

The goal is adaptive local surveillance — that is to say, surveillance objectives and modalities adapted to the cholera situation at the local level. Local surveillance units are country specific and should be administrative units no bigger than an NCP operational unit. In the absence of a confirmed cholera outbreak, the surveillance objective is rapid detection, investigation and response to a suspected or probable outbreak to interrupt the onset of local transmission. In a confirmed outbreak, it is to monitor morbidity, mortality and affected populations and inform targeted interventions that mitigate impact and spread and eventually end the outbreak.

Increasing the accuracy of surveillance requires systematic strategies for testing adapted to the cholera situation at local level. These should include expanded RDT use for early outbreak detection and outbreak monitoring, alternative recommendations if RDTs are not available, and more specific recommendations for culture and PCR use.

RDTs meeting satisfactory performance should become more widely available, making them a more viable tool to enhance the short term accuracy of cholera surveillance while increasing capacities for confirmatory testing in the longer term. RDT are to be used mainly at primary health care level for outbreak detection in surveillance units with absence of a confirmed outbreak, monitoring incidence trends in surveillance units with a confirmed outbreak, and as a tool to triage samples for further laboratory testing.

Systematic implementation of confirmatory tests requires increased testing capacities in laboratories. At present, confirmation by culture is not always performed and it is not always clear what is considered as a positive culture result; lab culture results are not always reported up to national level; and, while PCR has been introduced in a few laboratories, there is no consensus on the situations requiring PCR testing, or on the method to be used. To counter this the GTFCC interim surveillance recommendations include recommendations on the regularity of testing.

The presentation outlined the recommendations for testing in surveillance units with absence of a confirmed cholera outbreak (Figure 6) and in surveillance units with a confirmed cholera outbreak (Figure 7)

Figure 6: Testing recommendations for surveillance units with absence of a confirmed cholera outbreak

	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**

Figure 7: Testing recommendations for surveillance units with a confirmed cholera outbreak

	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

The next steps in developing these recommendations are operationalization, with the GTFCC supporting countries implementing the recommended strategies and addressing country feedback. The comprehensive update of the GTFCC guidance on cholera surveillance, expected by end 2023, will include:

- testing recommendations for a comprehensive adaptive surveillance framework (including additional clustered transmission and community transmission cholera situations);
- a didactic "use case" of probable cholera outbreak definition;
- further operational guidance (e.g., on inconclusive RDT results, RDT use in the context of CBS, specimen storage, safety and quality, etc.); and
- minimum performance targets for routine monitoring and evaluation of cholera surveillance, including testing.

Gavi support for cholera diagnostics

***B. Evans** & **L. Hampton**, Gavi*

Gavi supports health system strengthening and vaccine procurement, including for cholera, under a model that requires countries to cofinance vaccine procurement, with the amount of cofinancing determined by

their income group. Countries will eventually need to assume financial responsibility, but diagnostics support currently has no cofinancing and will not until at least the end of 2025. Gavi funding for health systems improvements can include cash support for surveillance (although this is not linked to diagnostic applications). 57 countries are currently eligible for new vaccine introduction support, including for diagnostic tests, and these include most countries on the GTFCC Roadmap.

Gavi diagnostics support aims to improve national diagnostic testing capacities and enhance epidemiological data to improve vaccine support effectiveness, efficiency, and equity. It focuses on market shaping to ensure the availability of fit-for-purpose diagnostics and funding for procurement of diagnostics in eligible countries. The Gavi Board has approved a US$ 55 million envelope to support diagnostics across all six target disease areas during 2022-2025.

RDT pilot studies are currently taking place across DRC, Niger and Nepal to improve understanding of RDT testing strategies and assess the effectiveness and feasibility of alternative RDT deployment strategies across a range of incidence settings, the results of which are expected by the end of 2024. The outputs of these studies may be used for future revisions on surveillance guidelines, and Gavi will use them to inform revisions to cholera diagnostics support and guidance.

Gavi aims to open applications for Gavi cholera diagnostics support in June 2023. Distribution of applications is expected to start in mid-June, with an application deadline in mid-July. Applications received by mid-July could result in RDTs being shipped to countries by the end of 2023. In 2024, Gavi expects to revise its materials (and potentially the scope of support) alongside revisions to other GTFCC guidelines. For now, the confirmed scope of support is funding for procurement (with no cofinancing requirement) of cholera RDTs. There is no directly-linked cash or operational support, but other Gavi cash grants (such as those for health systems strengthening funding), can be used for this purpose. Requirements for applications include a calculation of the number of RDTs required per year and documentation of country readiness to introduce RDTs. Gavi plans to buy Arkray and Abbott RDTs in the short-term, with a preference for WHO prequalified product(s) in the longer term, following a proposed RDT quantification approach that builds on GTFCC RDT interim guidelines to produce annual national demand.

An Excel tool has been built to test this approach, based on information in NCPs and other health facility data. This has estimated demand for a number of countries including Kenya (62 000 RDTs), Ethiopia (270,000) and Bangladesh (210,000). If countries have alternative quantification methodologies to estimate demand, these can be used instead.

Gavi is requesting country input to refine application materials, and volunteer countries to apply in the first round. Those interested should reach out to bevans@gavi.org and lhampton@gavi.org; a draft package of materials will be shared for offline review, containing funding guidelines, the proposed application form and the quantification approach.

Further ahead, Gavi anticipates expanding cholera diagnostics support to include PCR testing, though this will require target product profiles (TPPs) and the availability of validated products, as well as an operational approach. If this is of interest to the GTFCC and countries, Gavi hopes to organise follow-up meetings to discuss the next steps.

Gavi will continue to ensure its materials complement GTFCC surveillance recommendations, and will work together with the GTFCC through the upcoming revisions of its materials. Gavi will also continue engaging manufacturers, in the expectation that Gavi procurement of cholera diagnostic tests may increase interest in among manufacturers, leading over time to development and availability of improved commercial cholera tests.

Serologic data for cholera surveillance and control: where are we today?

***A. Azman**, Johns Hopkins Bloomberg School of Public Health*

Counting cholera cases is difficult because of the low specificity of the definition of a suspected case and the imperfection of diagnostic tools. Seroepidemiology for cholera is challenging because cholera serology is different from that of many other vaccine preventable diseases, due to factors including faster decay; variable baseline levels and high variability in post-infection antibody trajectories.

Differences in the boost and decay of different antibodies are helpful in estimating recent infections. Seroincidence is another useful approach. Laboratory methods offer a range of options, including vibriocidal (functional) assays and luminex assays (or ELISAs). In partially vaccinated populations, there is a differential antibody response between vaccinated and infected people in the first few months. Recent infection models can be adjusted if vaccination status is known, and after waiting approximately three months post-vaccination, models no longer misclassify vaccinees as recently infected.

After exploring a number of case studies of the use of serology to generate national overviews, including examining the infection-to-case ratio in Haiti and the preliminary insights generated by combined serologic and clinical surveillance in Bangladesh (~800 infections for every medically attended true cholera case, ~160 infections per symptomatic infection and ~5 symptomatic infections per medically attended true case), Dr Azman summarized the current situation for serology in cholera surveillance and control as follows.

Laboratory methods are available in multiple labs, including the use of Luminex beads, and analysis methods allow for estimation of seroincidence rates in the past six months (and less reliably up to a year). With sufficient care, serosurveys are feasible in partially vaccinated populations, and work to characterize seroincidence is ongoing in several locations including Nepal, DRC, Bangladesh, India and Cameroon.

There is a need for further standardization of analysis tools through improvements in luminex data processing, better availability of standard reagents (e.g. beads) and standardization of seroincidence estimation. More work is needed to examine what conclusions can be drawn from seroincidence data, especially in highly endemic settings, and data on levels of exposure versus infection. There is a need to study how this can be translated into conclusions about immunity, and whether this varies by setting. All of this may be made more feasible and more enjoyable by the increased opportunity to collect large amounts of serologic data using new multipathogen serosurveillance platforms.

It is also possible to capitalize on other efforts: for example, a lot of investment is currently going into multipathogen serosurveillance, to which it would be inexpensive to add cholera work, and many actors are already doing this to gather diverse serologic cholera data from a range of different places. Others – PAHO, for instance – are thinking about generating toolkits and resources for integrated serosurveillance, and since the COVID-19 pandemic there has been a huge increase in publications mentioning serosurveillance. All this activity gives the GTFCC a valuable opportunity to capitalize on other work, collect data to complement clinical surveillance data, and improve the picture of what is happening in communities.

A period of discussion raised a few more points.

- While the value of this approach is yet to be confirmed, many people have shown that the Luminex works well on dried blood spots for many different antigens. Data has been collected from DRC and is being analysed to confirm whether this is viable for cholera. Dr Azman's team are optimistic.
- There were questions about whether work is being done to look at shedding and whether people who have frequent exposures are infected, and the bigger question of whether they are actually protected. One way to measure that might be to look at whether people that have these boosts shed *Vibrio cholerae* in their stool. Some data from household studies in Bangladesh show that people do shed asymptomatically. A number of ongoing studies may provide further insight.
- In countries with high seroprevalence there are two main public health use cases for serosurveillance. One is to track the level of seroincidence across all settings, looking at trends and providing a complementary indication of how exposures change over time – particularly if WASH conditions improve. The other is to use serosurveillance as an additional input into the PAMI mapping process, providing data that are less biased by care-seeking and health systems weaknesses and/or geographic variability.

Conclusion

Philippe Barboza & ***Flavio Finger***

Drs Finger and Barboza closed with a few summary observations. The meeting produced useful feedback, all of which will be taken into account as future versions of the surveillance guidelines, testing strategies and other resources are developed and refined. The GTFCC is grateful for all the input from attendees, the enlightening presentations of the speakers and panelists, the technical and logistical assistance of the Fondation Mérieux, the ongoing efforts of the working group members and the generosity of the Ministry of Health of Mozambique for hosting this meeting.

Closing remarks

Q. Fernandes*, Mozambique National Director of Public Health*

Dr Fernandes closed the meeting with a short speech expressing gratitude to the GTFCC members and meeting participants. He expressed the view that the global upsurge in cholera cases and the pressures of poverty, vulnerability and climate change should be seen not as fatal issues, but as a call to accelerate common efforts to eliminate cholera – a goal he felt was possible. He pointed out that surveillance would be the cornerstone of the necessary prevention and control strategies, especially in countries with limited resources. These include Mozambique, where implementing cholera control activities effectively and sustainability remains challenging.

He noted the tremendous collective work to address these challenges, including the recent development of new guidance and tools, and expressed the hope that community surveillance systems would be given appropriate importance in future, as foundational elements of effective, timely, responsive surveillance systems.

Dr Fernandes ended by paying respect to the high level of country representation at the meeting, both in Maputo and online, and underlining the invaluable importance of openly sharing experience, difficulties and lessons between countries. Despite differences in context, the whole community shares similar challenges, questions and goals. Cholera respects no borders, and timely sharing of surveillance data between countries, regions and across the world is essential to informing preparedness and readiness activities: together, we are better prepared.

Dr Fernandes ended by reiterating Mozambique's engagement in the fight against cholera.

Laboratory working group

Welcome and opening remarks

***M.L. Quilici**, Institut Pasteur and chair of the GTFCC Laboratory Working Group; **P. Barboza**, GTFCC Secretariat, WHO Cholera Technical Team; **N. Mabunda**, Director of Public Health Laboratories Mozambique.*

Dr Quilici opened the laboratory working group meeting with a short welcome to all present, in person and online, before Dr Barboza stressed the importance of finding ways to use the different elements of laboratory diagnosis to aid the fight against cholera.

Achievements of the GTFCC Laboratory Working Group

***M.L. Quilici**, Institut Pasteur and chair of the GTFCC Laboratory Working Group*

The GTFCC Laboratory Working Group has several aims. These are to provide strategic guidance and set minimum standards; provide tools; support training for lab personnel on testing and testing strategies; improve performance and speed; support not only central/reference labs but also peripheral labs (particularly around PAMI); provide quality assurance and progress evaluation; map existing capacities and link the mapping with epidemiological data to identify lab needs around PAMI; identify needs in this area and make the necessary links with donors; identify mechanisms for provision of equipment and supplies; create links with, and promote, regional and subregional lab networks, to improve preparedness and coordination and to investigate cross-fertilization with the work of other disease fields; and promote the strengthening of bacteriology labs in general. To date, the working group has focused on providing guidance and standards and providing tools, with ad hoc progress in other areas.

2022-2023 has been a busy year. The working group has grown, welcoming new organizations and institutions. 2022 (Figure 8) saw increased focus on finalizing long-standing activities, while 2023 to date has been about resuming regular work in the difficult context of a global cholera crisis. Members of the GTFCC laboratory and epidemiology working groups also worked jointly on updating the surveillance guidelines for cholera.

Achievements for the past year included the development of the October 2022 Guidelines on Environmental Surveillance for Cholera Control (available in English at https://www.gtfcc.org/wp-content/uploads/2022/10/gtfcc-technical-note-environmental-surveillance-for-cholera-control-october-2022.pdf and in French at https://www.gtfcc.org/wp-content/uploads/2023/06/gtfcc-technical-note-environmental-surveillance-for-cholera-control-october-2022-fr.pdf)); completion of the February 2023 Interim Guidance on Public health surveillance for cholera (available in English at https://www.gtfcc.org/wp-content/uploads/2023/02/gtfcc-public-health-surveillance-for-cholera-interim-guidance.pdf and in French at gtfcc-surveillance-de-cholera-lignes-directrices-provisoires.pdf), with the finalized, comprehensive recommendations expected by the end of 2023; and creation of a Job Aid (in English: https://www.gtfcc.org/wp-content/uploads/2022/10/gtfcc-job-aid-isolation-and-identification-of-vibrio-cholerae-from-fecal-specimens.pdf; in French: https://www.gtfcc.org/wp-content/uploads/2023/06/gtfcc-outil-de-travail-isolement-et-identification-de-vibrio-cholerae-a-partir-d-echantillons-de-selles.pdf) and accompanying Fact Sheet (in English: https://www.gtfcc.org/wp-content/uploads/2022/10/gtfcc-job-aid-isolation-and-identification-of-vibrio-cholerae-from-fecal-specimens.pdf; in French: https://www.gtfcc.org/wp-content/uploads/2023/06/gtfcc-fiche-technique-isolement-et-identification-de-vibrio-cholerae-a-partir-d-echantillons-de-selles.pdf) for the isolation and presumptive identification of *Vibrio Cholerae* O1/O139 from faecal specimens.

Activities that were not addressed this last year include the development of a Job Aid on methods of collection of stool specimens (in progress with JHU) and the development of PCR guidance (a high priority as no protocols or recommendations currently exist). The development of recommendations for AMR is currently on hold pending clarification of the needs.

New activities and those under consideration include a high priority project to develop recommendations in terms of minimum laboratory capacity standards for cholera affected countries as well as a comprehensive tool for assessing cholera laboratory capacity. The GTFCC secretariat has been granted US CDC funding to further these efforts through the recruitment of a consultant dedicated to finalizing the guidance and the tools and to execute assessments in four GTFCC countries.

The ideal next steps for the working group are to close the first chapter on document development and initiate operational activities including supporting broader, more systematic training for lab personnel; the mapping of existing capacities, in collaboration with donors, and initiating broader conversations about needs and mechanisms for provision; and connecting and finding synergies with regional and subregional laboratory networks.

Testing and confirmation of cholera

Moderator: ***A. Debes,*** *John Hopkins University*

Strengthening cholera diagnostics – molecular diagnostics

L. Hampton*, Gavi*

Gavi cholera funding support may be available for procurement of molecular diagnostic tests, greater use of which could improve targeting of OCV preventive campaigns. While RDTs are expected to be the mainstay of such testing, molecular tests can potentially help with quality assurance and assessing toxigenicity.

Cholera molecular diagnostic tests are also potentially useful as part of larger testing systems, with RDT testing decentralized and molecular testing done in reference laboratories. Molecular testing of samples of both positive and negative RDTs can be used to monitor RDT performance, the sensitivity and specificity of which have been shown to vary in different settings, indicating expected RDT accuracy in a specific setting and allowing adjustment of incidence calculated from RDT results to reflect accuracy in that setting. Molecular testing can also indicate cholera toxigenicity.

Gavi can potentially fund procurement of a range of supplies for cholera molecular testing: if the necessary conditions are met, these could include validated commercial cholera molecular diagnostic test kits, consumable supplies such as centrifuge tubes and pipette tips, and equipment. As with Gavi's vaccine funding, governments will eventually need to fund this, but transition of financial responsibility is expected to be gradual, with cofinancing starting a few years after the beginning of Gavi support. Tests would be accessible at UNICEF prices to all countries.

To facilitate Gavi support for procurement of cholera diagnostics, certain things need to happen. These include development of TPPs and test evaluation protocols for molecular test kits; evaluation of those kits and identification of the kits worth scaling up; development of clear guidance on how to distribute molecular test kits and supplies across a country (efficiency will be critical because financial responsibility for procurement will transition to countries); and submission of country applications for Gavi support. Gavi's experiences with yellow fever diagnostics show that this model can work.

Experience with molecular diagnostics and cholera

Cholera genomic surveillance in Lebanon

***G. Matar**, American University of Beirut*

The American University of Beirut is home to the WHO Collaborating Centre for Reference and Research on Bacterial Pathogens, which performs laboratory cholera testing to detect cases, confirm alerts and declare outbreaks, monitor antimicrobial susceptibility (AST), characterize circulating strains, identify changes in virulence, support epidemiological investigations and declare outbreaks ended. Terms of reference include training national and regional staff and collaboration with other stakeholders.

The tests used are the traditional phenotypic detection methods, RDTs and culture; traditional molecular detection methods of *Vibrio cholerae* through nested multiplex PCR panels; biotyping; AST; traditional and advanced genotyping methods; pulsed-field gel electrophoresis (PFGE); and whole genome sequencing (WGS).

After explaining how these methods are implemented, Dr Matar presented an example cholera surveillance report for Lebanon, dated 24 January 2023, with cases disaggregated by factors including locality, sex, hospital admission and outcome.

Antimicrobial susceptibility testing has been done using disc diffusion assay validated with broth microdilution (BMD) assay on 68/300 pure cultures showing *Vibrio cholerae* isolates, and it has been shown that cholera in Lebanon has become resistant to ciproflaxin. Azithromycin is therefore now the main recommendation, with doxycycline another option.

Lebanon is capable of concurrent detection and full characterization of *Vibrio spp.* using WGS relying on genomic DNA extracted from bacterial isolate, identifying serogroups, biotypes, virulence determinants, AMR genes, and the presence of plasmid and/or bacteriophages in a single run. This provides the highest resolution genomic typing method that can compare samples to source and construct phylogenic trees. Lebanon expects the cost of WGS to drop dramatically in future once its use as a diagnostic tool becomes more widespread, making it the future of lab-based surveillance of microbes implicated in outbreaks.

Bangladesh: an icddr,b perspective - cholera detection and *Vibrio cholerae* isolation and characterization

***M. Alam**, International Centre for Diarrhoeal Disease Research (icddr,b), Bangladesh*

Dr Alam presented the cholera detection methods in use by the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b), explaining how various methods worked and drawing attention to some of the papers his team have published. The lab is capable of cholera detection using a full range of methods including WGS.

A joint Environmental Genome Project of *Vibrio cholerae* is ongoing at icddr,b jointly with Sanger institute (UK) & PGIMER (India) and is the largest whole genome project in the world using *Vibrio cholera* isolated from the environment. Another icddr,b project used whole-genome analysis of clinical *Vibrio cholerae* O1 in India and Bangladesh to reveal two Asian lineages: the first, lineage 1, is predominant in Bangladesh and found in other countries of Asia; the second, lineage 2, is dominant in India and is found in Syria and Haiti. It is important to work with WGS and live bacteria to understand drug response and other important phenotypic characteristics when designing or targeting interventions.

Cholera in Uganda: a molecular diagnosis journey

Namubiru Saudah Kizito

Cholera is now endemic in Uganda, but culture diagnosis was started there in 1968 as a preparedness measure before the first outbreak in 1971. PCR came into use in the 2000s, around which time RDTs were also being piloted. LAMP assays were introduced in 2018 and are still under validation, and Uganda is yet to start using genomics for surveillance. For now, microbiological culture remains the gold standard.

Turnaround time (TAT) is 3-4 days from plating onto selective agars, sequential subculture, and cytotoxic (CT) production test. This can be carried out in nine public laboratories and a few private laboratories across the country, and regions lacking the necessary capacity refer samples to the national microbiology reference laboratory (NMRL). Uganda has nine AMR sentinel surveillance laboratories and a robust sample transport network built around 100 hubs connected to over 3000 health facilities by motorbike. Sixteen vehicles move samples from hubs to reference labs, allowing Uganda to transport over 2.5 million samples per year.

Rapid diagnostic tests are used in Uganda mainly for screening, but are not yet rolled out. The test currently in use has been used since 2018 and it still being validated. All samples are still referred for reference testing irrespective of the result.

Conventional PCR assays have been in use since 2000, mainly for studies though they also serve a public health function. These tests are currently used on demand and are done at National level and research laboratories only. They use the Gel electrophoresis method and TAT is approx. 3-4hrs.

LAMP assays are currently being validated; while these are still used in research mode it is hoped that they will bring future advantages including shorter TAT; ease of use; and the possibility of field deployment.

So far Uganda has learnt several lessons. Molecular techniques remain expensive in terms of supplies, equipment and the cost of developing or acquiring the technical competences necessary to use them properly. While culture remains the gold standard, TAT is still too long, especially in outbreaks. Immunological assay RDTs are promising, but the RDT that is currently available is still to be validated. Many of these problems could be alleviated through dedicated funding for molecular diagnostics and surveillance.

In conclusion, Uganda has made great strides in cholera diagnostics since the early 1970s, and RDTs could be another step forward, offering an even more acceptable and cheaper option at point of care if they can be validated in the Ugandan context. Molecular techniques, especially the LAMP, are promising assays but they still need to be validated and rolled out, even for routine testing. Genomics is an area for possible growth, but while Uganda has the capacity for genomic testing, cholera is yet to be included in the programme.

Testing and confirmation of cholera (continued)

Cholera molecular diagnostics: research to outbreak confirmation

***A. Debes**, JHU*

Existing GTFCC guidance on testing includes a 2017 technical note on DNA-based techniques for identification and characterization of *V. cholerae* strains using conventional and qPCR tests; DNA-based techniques for advanced genotyping of *Vibrio cholerae* strains; and shipment and storage of samples. Development of a job aid to accompany the latter is in progress.

Future recommendations may also address methods for sharing equipment and working together (in most countries, real time testing equipment supplied for Ebola and COVID tends to be at fixed locations in virology labs, and thus unavailable for other uses or transfer to bacterial and/or enterics labs). Both conventional and real time methods should be part of any new GTFCC recommendations.

The gold standard testing combinations are as follows. In surveillance units where there is no confirmed cholera outbreak, the testing algorithm is designed around 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, the algorithm is designed around any person infected with *Vibrio cholerae* O1 or O139 identified by presumptive identification (culture/seroagglutination) or PCR.

PCR should be specifically recommended for toxigenicity testing in very specific situations.

There is a need to review how PCRs are recommended for toxigenicity testing, species identification and serogroup identification (O1/O139), as well as to design implementation guidelines. These will have to be based on assessment in context of the current (regularly) practiced bacterial molecular work methods; the relevant pathogens; and existing equipment and its availability. The availability question must also consider the possibility of access to the equipment for bacterial work— including whether it must be shared with viral pathogens, and whether the same laboratory personnel can work on bacteria and/or viruses and parasites. Training gaps must also be assessed. Input is therefore invited current 2023 testing strategy, including specifically around the timeline to implementation, how to enhance understanding of cholera disease burdens, elimination contexts, and any additional PCR suggestions for the new recommendations.

Work is also needed on a new molecular testing strategy. Currently, it is expected that cholera PCR capacity is often only found at national laboratories, and conventional PCR methods are often developed in association with research projects. This picture may have been changed by the pandemic: post-COVID, qPCR machines may be more widely available. It is therefore necessary to assess how available they are, whether they can be used for work on bacterial pathogens, whether they might be used regularly for cholera confirmation, and therefore whether they could be implemented into national and/or regional strategies.

There are currently there are no WHO-prequalified commercial kits for cholera, which is usually cultured and often enriched in APW prior to culture, meaning that quantitative PCR is of questionable value. While qPCR machines and kits were not widely available pre-pandemic, there are now 5-6 commercial qPCR kits and more being created.

The topic of in-house testing requires discussion of standardization of primers / probe sequences and whether WHO should create a standard by which to facilitate comparison and/or reporting of findings with in-house or commercial kits.

A range of commercial kits are also available, and the working group would be keen to hear about any experiences with these.

In summary, Molecular Diagnostics are being added to the GTFCC Testing Strategy, and the working group will need to collaborate with country partners to help establish PCR capacity and related needs around training, supply chains and equipment. There is also a need for a TPP and independent validation capacity.

Discussion

A brief period of discussion allowed participants to share a few country and regional experiences in molecular diagnostics, and make a range of different points.

- Given the widespread logistical challenges, including with RDTs, there is a need to analyse exactly how molecular diagnostics will enhance understanding of cholera disease burden, and whether the target is to increase the number of positives by doing PCR to target OCV and work towards elimination, or to enhance overall bacteriology given the current focus on viral pathogens.
- In the Eastern Mediterranean there is a huge disparity in country capacities. Some countries have access to everything; others have complex emergencies. A lot has been done in the latter by WHO and other implementing partners, especially in virology; but bacteriology remains relatively weak in central public health labs, which struggle with issues of access to resources. Limited numbers of PCR machines mean the use of that technology is not routine and is often limited to outbreak confirmation. PCR reagents for bacteria including cholera are often unavailable. The region has no local market and even well-resourced countries must depend on international markets. WHO has a hub in Dubai that procures and dispatches supplies to countries in the region, though this is hampered in some places by a lack or absence of commercial flight options – for Yemen, for example, where needs are acute, flights may be limited to once every four months.
- Somalia uses PCR for COVID and influenza but not cholera, because of a lack of access to reagents and capacity issues in the national lab, of which Somalia has only one. If there were a solution to the logistics barriers and training could be made available, Somalia might be able to implement some of the new interim guidance recommendations.
- Kenya is not currently doing PCR for cholera but using culture instead. The equipment is available – Kenya has a molecular lab – but issues and barriers include a lack of service contracts, reagents, capacity and funding. Refresher courses for lab personnel would be very useful, as Kenya has a very good genomic sequencing lab but is held back by a lack of funding. For example, Kenya had planned to implement genomic sequencing for its current outbreak and gathered more than 150 samples from different sites, but the expected support was withdrawn so the project could not continue. If the supply chain were improved, Kenya would be able to do PCR and WGS.
- WHO has encouraged countries across Africa to integrate systems rather than default to vertical programmes. During the COVID-19 pandemic, molecular capacities were built in many countries and now WHO is encouraging Member States to leverage and build on them. The biggest challenge is one of logistics and supplies – and this has been the case with RDTs as well. Gavi's investment in diagnostics is welcome.
- It is a common assumption post-COVID that qPCR machines are now more widely available than conventional PCR. There are pros and cons to both: conventional is cheaper and some reagents are more easily accessible, whereas qPCR does not require a gel, with all the issues that implies. In addition, there are issues to consider around in-house versus commercial kits. Gavi will support commercial kits, but they will need to have a recommendation from a WHO expert group.
- RDTs are for the rapid response teams more than labs, but the guidance addresses labs. In field contexts there is a need for other guidance, especially around waste management and sample management. The testing strategy is not currently viable in the field in some of the more challenging national contexts: in an outbreak, doing molecular testing on a given number of RDT positives is challenging or impossible, and when it is possible it takes too long and produces confusing results. Sample management is a huge issue. If supply problems can be solved, the Eastern Mediterranean and African regions can use their respective hubs in Dubai and Kenya to ease distribution to countries; but use of PCR in labs that are not adequately proficient is not correct for these contexts.
- Some national labs have shifted to in-house options for arboviruses because logistics are easier to manage.

- Ignoring costs and other considerations, LAMP may be easy to use, can be deployed in mobile setups, and allows faster competence and training. The biggest drawback is the cost.
- PCR is very sensitive to contamination, but the meeting heard from one country lab with a positive pressure room specially designed for qPCR, into which only the person operating the procedure is allowed to go. Most countries do not have equivalent facilities.
- Experiences in Bangladesh suggest that it is important to be careful about which brands and sources a lab uses, as specificity and sensitivity can vary. Not all RDT positive samples give culture and/or PCR positivity. Multi-method support is an important asset.
- As the recommendations are updated, it will be necessary to revisit the cholera kits recommended by WHO, which currently do not mention PCR at all. This process has not yet started.
- Johns Hopkins will soon evaluate a number of in-house qPCR and commercial PCR kits. There was some suggestion that WHO or the US CDC might establish a set of standards for in house assays.
- Very few people – if any – in the GTFCC have yet had sufficient experience with commercial qPCR kits to outline issues on their costs, ease of use and training requirements.
- CDC experiences suggest that the implementation burden depends a lot on whether those being trained have had any experience using molecular methods – this has a significant effect on the amount of time required for training.
- Experience from the Eastern Mediterranean region suggests that use of commercial qPCR kits is very easy; but in-house approaches require a lot of training. Regional WHO collaborative centres had to support the expansion of molecular methods during COVID because many lab staff had no understanding of the basics of PCR work. This training has made a big positive difference.
- There were some requests to include long term economic/cost-benefit analysis in the guidance, along with some aids to understanding of supply chains.
- It was pointed out that the number of tests that are recommended and done has an impact on the market size and therefore on the willingness of commercial producers to produce the kits – an important thing to remember when arguing for fewer tests to be done.
- There was discussion of the use of MALDI-TOF; US CDC was doing an internal validation of this approach at the time of the meeting, including Vibrio cholera and other bacterial enteric pathogens. MALDI-TOF is only as good as the comparative database that is used, the references in which have great influence on results. The most widely used system broker also does not include cholera, meaning an additional database has to be bought, and buyers must prove their capacity to work on such dangerous pathogens.
- GenExpert was also suggested, which has the benefit of widespread availability. No cholera cartridge currently exists for this platform, but during Gavi outreach to manufacturers Cepheid indicated that they are thinking about developing one. This is not yet on the table, but it could be, especially if progress can be made with TPPs for molecular diagnostics for cholera.

Conclusions

The moderators summed up the session with a few takeaways:

- There is still some work to do to bring molecular capacity into cholera confirmation and testing across public health network, including focused attention on testing supply chains and equipment.
- As the process of TPP generation and validation continue, it will be possible to have more substantive discussions about commercial kits.
- The guidelines are not revolutionizing cholera diagnostics, or suggesting all samples be tested using PCR, or even suggesting that regular proportions of samples be tested using PCR. Instead, they try to open a window to new diagnostic algorithms, avoiding being too prescriptive and remaining open to a range of possibilities.

- The new recommendations do recommend testing for toxicity, which does currently require PCR, but this part of the requirement only applies to specific samples. Methods for circumvention are written into the guidance, including using partnerships with other laboratories that have the required capacities.

RLDT - A rapid and simple molecular diagnostic assay for cholera, applicable to endemic countries

***S. Chakraborty**, Johns Hopkins Bloomberg School of Public Health*

The existence of a simple, rapid, sensitive and specific diagnostic test for cholera would facilitate rapid outbreak responses of all kinds (treatment, OCV and WASH) and provide reliable surveillance data to guide long-term policies and interventions. Current options are suboptimal: microbiological stool culture is the current gold standard but requires 2-3 days TAT, appropriate lab facilities and trained personnel; PCR is not widely used or available, offers several unstandardized methods with no validated technique, and requires reagents, competent laboratory support and technical skills; and several studies and systematic reviews of RDTs have reported performance characteristics that do not meet the minimal performance recommended by the GTFCC.

The rapid loop-mediated isothermal amplification based diagnostic test, RLDT, offers a solution. It detects cholera ctxA and O1rfb directly from stool in less than an hour; it can be performed on fresh, frozen or dried stool on filter paper, or rectal swabs, and on environmental and drinking water; and its lowest detection limit is 4x104 CFU/gm of stool. Further advantages of RLDT include simplicity (it is performed directly from stool with minimum treatment and a hands-on time of five 5 minutes; speed (less than an hour from stool to result); sensitivity (LOD: ~104CFU/gm of stool); specificity (six primers are used for detecting each target); use of dry formulations that are stable at ambient temperature, do not require cold chain, and can be used mostly without electricity; a lack of need for reagents, as LRTs are already filled with dry reagents and primers, and all reagents and required plastics are provided in the RLDT kit; ease with which results can be read (results are provided via a battery-operated handheld reader); minimal need for equipment (only a heat block and a reader); ability to perform downstream applications; and semiquantitativity. Once a site is trained and has the reader, the RLDT can also detect Shigella spp, enterotoxigenic E. coli, Campylobacter spp, Salmonella typhi from blood and stool, and norovirus. RDLTs have been implemented for surveillance and epidemiology in Zambia, Burkina Faso and Bangladesh.

A field evaluation of RLDT for Cholera in Uganda, Bangladesh, Nigeria and India tested 665 samples across all four sites. Of these, all but eight culture positives were also positives by RLDT (a sensitivity of 97% and specificity of 79%); of those eight samples, five were also negative by PCR (a refined sensitivity of 99%). PCR vs RLDT revealed sensitivity of 97% and specificity of 93%. Ongoing implementation of Cholera RLDT in Nigeria, Uganda and Bangladesh involves provision of RLDT training in central labs in each country, which then train a further two national health facilities.

In summary, RLDT is a simple assay that can be applied to cholera endemic countries; it is more sensitive than RDTs and culture; it has shown excellent sensitivity and specificity for detection of cholera; it can be implemented at primary health care facilities; and it is ready for large scale production. RLDT therefore warrants broader application and evaluation as a culture-independent, simple and rapid diagnostic test.

Laboratory capacity and competency

*Moderators: **N. Wauquier**, Laboratory focal point GTFCC secretariat & **M. Turnsek, US CDC***

Laboratory Working Group workplan for 2023

***N. Wauquier**, Laboratory focal point GTFCC secretariat*

GTFCC guidance on minimum capacity standards for cholera laboratories must describe the least permissible condition required to demonstrate a basic level of performance. These standards could be considered as the first targets for overall strengthening of cholera lab capacity. Any new guidance must be in alignment with all current and future recommendations of the GTFCC. Recommendations must be described for all components of the laboratory system; should include sample transport, use and storage of supplies, etc.; must describe minimum standards at least at regional and central level; and should address the philosophical question of how minimal "minimal" is.

The next steps in the guidance development process will be to consult with the working group, countries and partners to develop a communal sense of what some of the minimum standards should be and where to set the thresholds; then to engage a US CDC-funded consultant to work alongside the working group and finalize the minimum standards.

WHO led a recent (2023) landscaping effort that used around 30 questions on current lab capacities to provide a "quick and dirty" capacity assessment and generate an initial sense of gaps and needs. Carried out in the global context of a cholera crisis, the results of this review informed several presentations in this session. Building on this and other past assessments, the working group is developing a toolkit to assess and map current capacity. Gathering this information offers great benefits including for advocacy and resource mobilization, helps map gaps and clarify intervention priorities, and helps target those laboratory interventions likely to have most impact on PAMIs.

The next steps on this front are to gather information on laboratory gaps and needs and reflect on how best to adapt the assessment tool to ensure that it captures them, and then to develop an assessment tool kit containing a questionnaire, user guides and checklists. This will then be piloted in four priority countries in a project funded by the US CDC and led by the GTFCC Secretariat.

Laboratories, gaps and needs for cholera testing: WHO regional overview

Africa

***F. Athanasius**, WHO Emergency Hub, Nairobi*

WHO's rapid assessment of cholera lab capacities, resources and opportunities classified five countries in the African region as Category 1 countries (Botswana, Malawi, Mozambique, South Sudan and Zimbabwe) and a further 18 in Category 2 (Algeria, Benin, Burkina Faso, Burundi, Cabo Verde, Cameroon, Chad, DRC, Equatorial Guinea, Ghana, Mauritania, Niger, Nigeria, Sierra Leone, Togo, Republic of Congo, Zambia and eSwatini). Figure 9 describes needs across labs in category 1 in terms of training and supplies.

Figure 8: Laboratory training and supply needs – category 1 countries, African region

Specific Areas of Training Required	Immediate Needs in Terms of Supplies	Lists with Justification of Request
Sample handling and processing of stool samples suspected for Cholera and other stool pathogens	Stool containers, transport media, Culture media (TCBS), *Vibrio cholera* antisera for O1 and O139 and types Inaba and Ogawa	• Build capacity for quality sample collection and handling • To isolate and identify causative agents of diarrhea • To differentiate between O1 and O139 strains of *V. cholera* • To determine the serotype of the Vibrio cholera
Stool sample collection, transportation, and handling and processing of stool samples suspected for Cholera and other stool pathogens	Cholera RDTs, Pasteur pipettes, media (Culture media-TCBS, transport media-Cary-Blair), peptone water, oxidase reagent, *Vibrio cholera* antisera for O1/O139, CT-SMAC	• To quickly diagnose and treat cholera • To ensure safe collection and transportation of specimens • To detect *Vibrio cholera* and other stool pathogens • Build capacity of testers
Culture and Sensitivity Training	Petri dishes, sample supplies, culture media, Antibiotics discs and other supplies	• To confirm *V.cholerae* and perform AST
Molecular testing (PCR, sequencing)	RDT kits, Culture media, Serological Antisera, PCR equipment, PCR primers, probes and other ancillary supplies	• To diagnose and monitor infectious diseases • To identify antibiotic-resistant strains • Detect pathogens that when culture resources are lacking

For the category 2 countries, the survey revealed gaps in areas including weak sample referral mechanisms, especially from remote areas; transport issues and frequent stockouts of culture media and reagents and long lead times affecting delivery; RDT shortages affecting testing strategies; lack of culture reagents for stool culture to rule out other differential causes of diarrhoeal disease; lack of technical capacity and reagents for genomic surveillance; training gaps affecting sample collection, handling, shipment/transportation and testing; a preponderance of old SOPs that do not integrate RDTs; missing kits and/or oxidase for antisera testing; lack of medium for storage of identified strains; frequent failures to renew certificates of IATA-certified shippers; and a lack of availability of PCR kits for strain identification and genomic sequencing inputs.

However, the survey also revealed a wealth of strengths that create manifold opportunities for cholera control and prevention. This included technical capacity for case detection and confirmation; the existence of job aids and SOPs for sample collection, packaging and transport; training on cholera sample handling and RDT testing; some prepositioning of transport media in hotspots; capacity for both culture techniques and drug susceptibility testing; existence in some countries of strong decentralized labs; some prepositioning of RDTs; microbiology laboratories validated for case confirmation; availability of conventional methods of enrichment and immunological tests with antisera; staff trained on safety and IPC procedures present in the field for sample collection, packaging, labelling, transfer and transportation; functional national systems for reporting laboratory results; and molecular capabilities including rtPCR, qPCR, SANGER sequencing and whole genome sequencing.

The region has experienced some challenges using Arkray Dipstick RDTs in the field. As well as the too-short shelf life, these have included the lack of marks on disposable plastic droppers indicating the amount of stool to be added to the tube where the strip is placed, or how much liquid should be added to tubes containing buffer. As too much liquid stool causes tests to fail and too little risks giving false negative results, this has caused problems. In addition, the provided package can only hold three Cary-Blair inoculated tubes; any more and it fails to close properly.

The next steps for the African region are to ensure Member States' understanding of the GTFCC strategy and ensure guidance is provided on differential tests. Countries will be supported to revise their testing strategies and address training gaps in sample collection, handling, shipment/ transportation and testing. Job aids will be disseminated, with work to ensure they are understood, and efforts will be made to strengthen subnational culture capacities for hard-to-reach areas, adopting efficient sample transport network models (such as the hub-spoke model used in Uganda, and/or use of contractors). Supply chain issues will be addressed, including through the use of stockpiles for reactive supply distribution. Resources will be mobilized for RDTs, culture, PCR and sequencing supplies and other supplies for differential diagnosis of other enteric pathogens. Existing virological molecular capacity and experiences will be

leveraged for PCR capacity building, and RDT/ culture data collection analysis and sharing will be improved.

Eastern Mediterranean

As previously mentioned, cholera capacities across the region vary widely between countries, and there has been little recent experience of cholera in most states, some of which have struggled. The meeting therefore heard brief sitreps from representatives of three Member States in the region which are facing particular problems with cholera.

Afghanistan is suffering from multiple outbreaks of different diseases including AWD, measles and COVID. Living and social conditions often make these diseases fatal, and the country is undergoing a complex and extreme health emergency. Afghanistan currently has one working public lab which is low on capacity and very understaffed. Existing staff are in need of further qualification, as they have to do testing for 17 priority diseases not even including cholera. Results are slow and expensive – without incentivising workers, reports are not done. This translates to poor capacity for testing for surveillance.

Even with WHO providing the region's consumables, training and capacity building, sample collection remains a challenge. Because of the prevalent health system conditions, when outbreaks occur in communities, people only refer to the health facilities at a very late stage—basically when they are about to die. Surveillance teams must therefore go to the field and collect samples, sometimes from places that can only be reached with more than two days travel in each direction. Sample collection is therefore very challenging and sample quality very poor – after such long travel times, using public transport as no other options are available, the majority end up discarded.

Reporting is another issue: Afghanistan does not have a reporting system to integrate lab results, and relies mainly on Excel sheets shared by email or WhatsApp. When feedback goes back to the field for case management, often the cases are already discharged without having followed treatment protocols.

The average length of time taken to procure supplies is nine months. Flights to Afghanistan have been unreliable and/or unavailable, and in the past sea transport in World Food Programme shipments has been the only option during outbreaks. On arrival the national food and drug authority can leave supplies in place for months before releasing them. Once they are released, cold chain is weak or nonexistent in many places. WHO uses its own cold chain for targeted interventions.

Afghanistan needs a great deal of support from WHO country and regional offices, for guidelines, technical capacity building, and establishing and building a system. The GTFCC is invited to pilot its guidelines in Afghanistan: there will be much to learn from efforts to adapt them to this very difficult context.

Somalia faces a similar situation, with the same problems as Afghanistan and additional issues around the lack of governance. Somalia has one national lab and a small number of trained staff – not enough for cholera testing. There is a large and unmet testing need that reflects the universally challenging nature of the health system as a whole.

WHO supports the country with reagents and supplies, but the bidding process is difficult and time consuming. The regional office would be assisted greatly if all the necessary supplies were included in the e-catalogue so the bidding process could be circumvented. Many countries in the region have no access to the market. WHO provides training for Somalia (and other countries) by sending people to Nairobi for training.

Lebanon has a lot of expertise, but faces many challenges and needs labs to support surveillance and response. At the beginning of the current outbreak, linked to the ongoing emergency in Syria, the strategy was to test all suspected cases, then to test cases and the environment around the positives.

This strategy required at least one national reference lab in the public health sector equipped to confirm cases using a range of methods, and WGS to identify the source of the outbreak. At the start the lab was not ready, due to a lack of resources, and a WHO Collaborating Centre offered support, allowing a welcome increase in the number of samples that could be tested.

The strategy has since changed to reflect the lessening intensity of the outbreak – ten cases are tested per week, 10% of which are cultured. In areas with no confirmed cases the approach is more aggressive: when a suspected case occurs, an investigation team is sent to collect samples and investigate patients and the environment. This strategy requires at least one lab in each province as well as the national lab, with strong capacity for testing, training and timely data sharing. Challenges to achieving this include the need to train staff, secure timely procurement, establish a proficient testing system that produces reliable results, and share data in a timely fashion with the Ministry of Public Health.

In future the strategy will change to test any suspected case, with two main approaches. One will be to respond to alerts from case reports, sending teams with RDTs to the field; the other will be to send screening missions to areas that have had cholera in the past. Lab needs under this model will be to maintain capacity and be ready for any new wave of cholera at national or provincial level, and to perform regular water testing. Challenges include procurement and sustainable access to resources. Once cases decline, donors will fall away, and it will be hard to maintain the resources needed for outbreak surveillance. High quality labs will have to be trained, equipped and assessed to support testing for surveillance and response.

Southeast Asia

Confirming AWD, especially cholera, is challenging in Southeast Asia because of limited availability of diagnostic tests and subnational laboratory capacity. Culture remains gold standard for confirmation, while RDTs are used in surveillance settings. PCR, molecular methods, toxigenicity testing and serology are done mainly in research settings. Confirmation is typically opportunistic in clinical settings, based on capacity, or done on a fixed proportion of AWD cases in surveillance settings.

Challenges include limited laboratory capacity for confirmatory diagnosis and limited availability of diagnostic tools such as RDTs and culture; the fact that PCR use for cholera diagnosis is not widely adopted because of the lack of trained personnel and the necessary resources; and the need to strengthen lab capacity and ensure wider availability of diagnostic tools in order to overcome these challenges and respond effectively to cholera outbreaks.

To overcome these challenges the region needs adequate funding and resources for capacity building in laboratories and procurement of diagnostic tests and equipment. Training and education are required for laboratory staff to improve their skills in AWD diagnosis and quality assurance, and collaboration and coordination among stakeholders need to be improved to develop and implement the diagnostic roadmap and other initiatives for AWD control. More timely and accurate data collection, analysis, and reporting are needed to inform decision-making and evaluate the impact of interventions.

Ways forward include development and implementation of a diagnostic roadmap that includes strengthening laboratory capacity for subnational AWD confirmation; ensuring that rapid response teams (RRT) are properly equipped to detect, investigate, and test suspected cholera cases by supporting transportation of samples to labs; and obtaining and stockpiling necessary materials such as RDTs, sample collection supplies, and laboratory reagents, including in districts not currently affected by cholera, to ensure preparation for potential outbreaks. Health staff need to be trained on laboratory diagnosis and sample collection (including use of case definitions, cholera testing strategies, and use of RDTs), using standard forms for data collection, data management and timely reporting, investigation and confirmation of suspect cases and sample collection and transportation. Genomic sequencing can be better leveraged to improved understanding of AWD transmission patterns; and quality assurance

measures can be implemented for testing and networking with existing capacities (such as WHO Collaborating Centres).

Resurgence of cholera in Haiti: National Public Health Laboratory (LNSP) gaps and needs

***K. Pierre**, Haiti Ministry of Health*

After the recent resurgence of cholera in Haiti, the Ministry of Health (MSPP) is committed to containing the outbreak. The Department of Epidemiology, Laboratories and Research (DELR) is responsible for providing information to support the response, planning and coordinating the response, and implementing a reporting system. The national response strategy is based on six pillars: case management, alert management, active tracing of contacts and other similar cases, epidemiological response, health education and monitoring and evaluation.

Major accomplishments to date have included reinforcing capacity for stool culture and AST in six regional laboratories; improving culture of stool specimens and the sensitivity of testing in the national lab (LNSP); central procurement of supplies for culture diagnostic capacity in subnational laboratories; testing of over 7000 specimens (including 2600 positives for *Vibrio cholerae*); achieving a turn-around time of two hours using Vitek2; developing the LNSP's capacity to detect cholera toxins using PCR; improving culture and AST capacity in regional laboratories; developing a national EQA programme; building genomic sequencing capacity at the LNSP; and procuring and installing Illumina MiSeq equipment.

Challenges include a difficult, unstable sociopolitical situation that creates difficulties transporting samples, fuel shortages and insecurity, including excessive turnover/departure of staff. Needs in Haiti are understandably many. They include sampling materials; supervision meetings and LNSP trainings to enhance decentralized culture capacity through designated subnational laboratories; laboratory reagents for AST; renovation of LNSP workspaces and three subnational laboratories; reagents for culture and small equipment for the 10 hubs performing culture testing; transportation; resources to send samples to international reference laboratories; training and supervision on collection of stool samples in selected sentinel sites; identification and training of two laboratory technicians to help with bacteriological testing and AST in the LNSP and two further technicians for each subnational laboratory; mentorship and training toolkits; support for development of an LNSP EQA programme for subnational laboratories; environmental laboratory capacity building to test water samples; SOPs and guides for water testing; and routine food hygiene and water quality surveillance.

Accomplishment of these goals could be helped by implementing external and internal quality control systems within the national network of laboratories that have the capacity to test for cholera and other acute diarrhoea pathogens; introduction of IT tools for epidemiological surveillance in subnational laboratories; and deployment of LIS in regional laboratories.

GTFCC Laboratory Working Group: vision for laboratory training

***M. Turnsek**, US CDC*

Laboratory training is critical to achieving the goals of the Global Roadmap. The benefits of improved training are many, and include increased capacity for lab confirmation; better information for decision making; more accurate, consistent testing and reporting; better development of staff and increased competence; improved preparedness and response; improved testing systems; and better confidence in results.

Current GTFCC resources to support laboratory training include job aids and fact sheets on the of RDTs, AST, isolation/identification of *V. cholerae*, specimen transport/packaging and strain conditioning; and technical guidelines on surveillance guidance, adaptive testing strategy, and reporting (including a reporting template). Planned future resources include a GTFCC laboratory training package with standardized material (presentations, training plans, checklists, etc.) available via the GTFCC website and online training courses available through Open WHO. Further suggestions on what the GTFCC can do to support laboratory training are welcome.

Proposed key training topics include the basics of cholera; specimen collection, preservation and transport; adaptive testing strategies; RDTs; primary isolation of Vibrio cholerae from stool specimens; strain conditioning for shipment and storage (short- and long-term); identification of toxigenic *Vibrio cholerae* O1 / O139; use of culture-based methods; molecular methods; AST; and data management and reporting. Suggestions for other topics are welcome.

There is also a need to clarify which health professionals and stakeholders should be trained in what across the health system, and how to structure training. The current GTFCC proposal is a tiered training plan in which the first tier covers (1) the basics of cholera, (2) specimen collection, preservation, and transport, (3) RDTs and (4) isolation and culture-based confirmation methods; tier 2 covers (1) adaptive testing strategies, (2) reporting lab results, (3) AST and (4) PCR; and tier 3 covers whole genome sequencing. Suggestions for other considerations or alternative options are welcome.

Formats and modes of training delivery must also be determined. These could include in-person or virtual offerings; onsite and external workshops; on-demand online courses; hands-on and/or lecture-based approaches; and internally or externally led courses. It would be useful for the GTFCC to know what approaches are likely to work best for partner laboratories.

Validating the training and measuring its success will be a crucial part of the programme. The success of tiered training programmes can be measured through stepwise certification at the end of each tier allowing participants to progress only once the previous tier is mastered. Recommendations for post training assessments include lecture-based training, whether in person, virtual or online, with before-and-after tests with real-time scores and feedback to correct wrong answers; and hands-on training/EQA wherein a technical partner or EQA provider sends a blinded panel for identification with reporting forms, instructions and a due date, and a subsequent performance letter may include a score. Recommended post-training competency assessments are customizable, can be organized internally, and can be tweaked to include different elements.

Experience from existing programmes: African Society for Laboratory Medicine (ASLM)

***A. Mataka**, African Society for Laboratory Medicine (ASLM)*

The ASLM is an association of public health laboratories with the vision of “a healthier Africa through access to quality laboratory services for all” and a mission to enable and empower national stakeholders to enhance the laboratory profession, practice, science, and networks. The ASLM aims for programmatic sustainability, leveraging over a decade’s experience and ability to lead programming and absorb support from global partners. The ASLM acknowledges that interventions must be tailored to fit different African contexts, focusing on solutions designed by and for Africans.

The ASLM has four strategic priorities:

1. refine and improve ASLM’s core technical strengths, focussing on the ASLM Academy, ASLM Conference, publications, and communities of practice to create and sustain knowledge hubs that facilitate knowledge sharing across the community;

2. build and organize the laboratory profession;
3. innovate and grow to stay relevant, across multiple disease areas; and
4. invest in people and systems.

In-service training is a popular intervention to address shortages in skills for health across Africa, but often fails to address clear norm-based targets, comply with recognised standards for educational quality, and/or formalize credentials properly – meaning its effectiveness in developing skills and competence in addition to knowledge is uncertain. The ASLM Academy (https://aslm.org/aslm-academy/) was launched in March 2020 to address these gaps, providing infrastructure to organize high quality training, delivery of associated credentials, professional registrations, continuous monitoring of workforce development, certification, continuous professional development (CPD) points and training packages, and courses and other educational activities.

Current opportunities available through the ASLM include a QWArS training curriculum, which provides training in a range of surveillance and epidemiology topics relevant to the GTFCC's work and goals. The ASLM is also engaging with cholera sequencing work in Ghana and Malawi.

The ASLM is also working to unlock the power of tiered laboratory networks through a lab mapping exercise across the Association's 15 Member States that has mapped 2291 labs to date.

Lab visits/Closed working group meeting

In this part of the meeting, a group of participants took the opportunity to visit a local laboratory and learn about Mozambique's cholera lab work, while the core Laboratory Working Group gathered in a closed session to plan its next steps.

Breakout sessions – refining the proposed minimum standards

During this session, the meeting separated into groupsto discuss three proposed minimal standards for lab capacities, then reconvened to hear summaries from each group.

The first group discussed National Laboratory capabilities, and recommended strengthening the proposed recommendations so that countries should have at least one laboratory operational and capable of isolating and identifying *Vibrio cholera* by culture **AND** PCR and performing AST and toxin testing. Both culture and PCR are required as culture alone does not allow identification. The lab should be capable of reporting results within a timeframe not exceeding seven days. There was some discussion of to where the lab should be obliged to report to the Ministry or directly to more peripheral teams in affected areas and the public health professionals involved in the intervention.

If PCR for toxin testing and antimicrobial susceptibility testing is not readily available in the country, mechanisms must be in place to refer supplies, samples or isolates for testing by an in-country partner or regional international reference laboratory. In this case, results should be reported within 10 days. This timeline may be more difficult and/or sensitive because of biosecurity challenges, technical difficulties in sample transport, permissions and logistics, and 10 days may be optimistic. There was some consensus that this timeline may have to be decided in-country by a central laboratory in collaboration with the GTFCC.

The second group agreed with the minimum standard of having at least one laboratory able to do culture and PCR, but in addition proposed that recommendations emphasize countries should consider regional or subnational capacity as an efficient way of improving the system where possible. This recommendation would necessitate engagement from the county at the highest level, but the group considered it reasonable and realistic.

The recommendations will need to address how to ensure that trained staff are always available to perform testing, helping leadership to plan human resources in advance so staff are ready when outbreaks occur. To evaluate the competency of lab personnel, at minimum the group suggested regular proficiency tests for staff and implementing internal quality assessments and internal audits in the lab/s. Competency assessments once or twice a year will be sufficient for permanent staff, with annual frequency the bare minimum, and the labs themselves can decide on the duration of their competency assessment for those people on contract and/or newly employed. To maintain quality during non-cholera times, labs can implement continuous quality improvement.

To sustain workforce resilience and help them to continue to respond to cholera, especially in times of intense pressure, political goodwill and good leadership skills are invaluable. Rewards and recognition for the efforts of staff during outbreaks also worked well during COVID in many settings.

Group three considered RDTs and national distribution plans. Their suggested minimum standard was for RDTs to be available in-country, prepositioned for ready access by designated end users, stored in adequate conditions and with consideration of expiry dates. These are to be used following GTFCC recommendations for the detection and monitoring of outbreaks, without out-of-stocks of reagents and supplies for more than two weeks in a one-year period.

The group agreed with the recommendations for RDT use in all contexts, but with some contextual adjustments. In the absence of confirmed cholera outbreaks, it is recommended that all suspected cases should be tested using RDTs, but consideration of varying contexts and the different case definitions in use in different regions led the group to expand this. In some places, where the case definitions are very broad, testing all with RDTs might not be sustainable in the context of supply shortages. The recommendation to test every suspected case with RDTs should therefore be adjusted based on the case definitions in use.

With confirmed cholera outbreaks and cases, the group agreed with the recommendation that in each facility/surveillance unit, the first three suspected cholera cases detected each day should be tested. There was a suggestion that the wording might be changed around “health facilities” and “surveillance units” to allow for different structures and political sensitivities in different contexts.

The group felt that the recommendations should be more prescriptive regarding where the RDTs should be prepositioned. As the location of the next outbreak can never be known, the recommendation should be for RDTs to be prepositioned at level two.

The group agreed that the minimum standards should address standards for sustainable supply chain for RDTs. This will have to vary depending on regional and national context.

The group agreed that recommendations should describe how to ensure that supplies are readily available to perform cholera testing. This rests on the previous questions (particularly re. prepositioning) and the network of national officers who link grassroots alerts of suspected cases with ministries and higher administrative levels.

Closing session

Dr Quilici addressed the session, thanking the translators, participants, organisers and all those who had made the meeting possible, and particularly the Director General of the National Institute of Health, Eduardo Guido, for his support for the meeting and for the GTFCC. She noted the positive atmosphere of discussion and collaboration, and emphasized the importance of having held a lab meeting after such a long period without one. Among themes that had emerged she noted the following issues and gaps that the working group would work to address:

- problems and shortfalls with human resources in labs, both with the numbers of trained staff and the level of their training;
- access to training for lab personnel;
- supply of reagents and consumables;
- preparation of labs in advance to handle crisis situations;
- lack of PCR capacity; and
- difficulties with sample transport and transport of reagents.

She ended on a note of positivity, expressing confidence that the working group and the wider cholera community would find solutions to these problems.

Closing both meetings, Dr Barboza again thanked Mozambique for hosting the meeting. This was the first time since the COVID pandemic that the GTFCC was able to organise a technical meeting in a country, and it provided a valuable opportunity to learn from the cholera control experiences of Mozambique, which has done massive work to strengthen epidemiological surveillance. He thanked funders and partners for keeping the community's work going.

He ended by emphasizing the importance of the lab sector: without laboratories, cholera control is blind and elimination is impossible. In the face of current considerable challenges, it is crucial to approach the work of building laboratory capacity in a stepwise, progressive manner – remembering that the job is not just about cholera. Efforts to support and build laboratories will be hugely beneficial for other bacterial diseases and for the fight against AMR.

Dr Barboza reminded the meeting that labs are not only responsible for providing results, but also for educating clinicians on how to interpret them and what to do with them – for example, clarifying persistent misunderstandings about positive tests versus treatment: laboratory tests are not required for treatment, which should be based on clinical data, but to testing what proportion of treated patients have cholera.

Eduardo Guido then officially closed the meeting on behalf of the National Institute of Health, underlining the importance of the GTFCC's work and expressing his pride that Mozambique had been able to host the meeting. Having such an expert group in Maputo provided extraordinary opportunities for country advocacy, and the GTFCC's presence made an important positive difference.

He sounded a note of warning: climate change will worsen in the coming years, and the most vulnerable countries will weather its worst effects. Mozambique is facing cyclones with ever-increasing frequency, with cholera outbreaks following immediately after, and recent years suggest seems that both the cyclones and the outbreaks are increasing in severity.

A key component in mitigating these outbreaks in Mozambique has been rapid early detection and declaration of cholera. As Dr Barboza said, labs are the cornerstone of cholera response – and so Mozambique has worked to strengthen its laboratory system. But there remains much to do, both here and elsewhere, and the GTFCC's work on recommendations and standards will be critical in the coming years.

Dr Guido is the chair of the regional technical advisor committee for southern Africa, a region with five collaboration centres, that has seen recent discussions about the establishment of regional task force for cholera control. He expressed hope for more advice and support from the GTFCC as the region started to build its local equivalent.

Dr Guido ended by noting the positivity of the meeting and the extreme productivity of the discussions, and expressed his certainty that the outcomes will exceed expectation.