



GLOBAL TASK FORCE ON CHOLERA CONTROL

GTFCC RESEARCH AGENDA – SCOPING MEETING

During the 5th Annual Meeting of the Global Task Force on Cholera Control (GTFCC) in June 2018, the Wellcome Trust and the UK Department for International Development (DFID) announced their potential interest in supporting the GTFCC research efforts. To initiate this work, Wellcome and DFID hosted a meeting with a small group of GTFCC partners on 23 and 24 July 2018 in London.

The objectives of the meeting were to reach consensus on a research agenda on cholera aligned with the GTFCC *Ending Cholera Roadmap*¹, and with the research agendas developed by each working group of the GTFCC.

A full agenda and list of participants are available in Annex 1. Group work was organised for most sessions and this document provides a summary of key discussion points and conclusions.

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OBJECTIVES AND EXPECTATIONS FOR THE MEETING

The meeting participants identified the following objectives and expectations for the two days meeting:

- Develop a research agenda on cholera that is strategic, aspirational, coherent and fundable, to be validated by the group
- Provide a crisper understanding of the problem statement
- Give a sense of priority and establish rough timelines
- The lack of partners able to implement research in difficult settings affected by cholera was also noted, as well as the opportunity to expand the group of partners involved and to identify key stakeholders to fill gaps. Partners also highlighted that the research agenda should leave space for innovation, high risk/“wacky, off the wall” ideas

LAYING THE FOUNDATIONS

Defining research was a first step to frame the discussions. The groups reflected on three key questions in the context of cholera: what does research mean, what is the value of research and how to prioritize research?

- Research is about gaining information to adapt strategies in order to improve the delivery of interventions. The question is how to best deliver cholera control interventions, to have the highest impact at the lowest possible cost.

¹Ending Cholera – A Global Roadmap to 2030: <http://www.who.int/cholera/publications/global-roadmap/en/>

- Research should focus on supporting the implementation of the *Ending Cholera Roadmap* globally with a strong focus on country level interventions. This means that the research questions need to involve strong buy-in from affected countries, with research also being country driven, to respond to field needs and not to researchers' agendas. It is therefore crucial to involve countries and to maintain the link between the research agenda and the implementation of the Roadmap. Participants regretted that countries representatives could not attend the London meeting - this was due to visa issues.
- The cholera research agenda needs to have a clear problem statement with clear objectives. Looking at what is done in the private sector, it would be useful to develop a critical path to 2030 to clearly identify what research is needed in the next 12 years – also looking at sequencing.
- One way to prioritize research questions could be to have a tiered approach - looking at importance and whether the results and impact are likely to be available in the near, medium, or longer-term.

IDENTIFYING THE KEY RESEARCH QUESTIONS – FEEDBACK FROM GROUP WORK

The sections below provide a summary of discussions held on the first day.

1. Presentations on the GTFCC Working Groups research agendas

The Chairs of the GTFCC Working Groups on OCV, WASH, Surveillance Laboratory, Surveillance Epidemiology and Case Management provided updates on the WGs research agendas. Presentations are available [here](#)

Below is summary of the discussion that followed.

- There are recurring themes across Working Groups and some key research questions on estimating the burden of disease, better defining cholera hotspots, the dynamics of transmission and risk of spread of the disease. Many questions focus on what happens at the community level: risk factors, transmission routes... and these questions are not limited to WASH. The concept of hotspots needs to be more critically evaluated – cholera is only diagnosed when there is an epidemic which creates a self-fulfilling prophecy. There are three key assumptions of the Roadmap to be validated:
 - Hotspots account for a major fraction of the burden of disease at the country level;
 - Elimination of cholera transmission is possible with WASH and OCV in hotspots;
 - Elimination of cholera transmission in hotspots will eliminate cholera transmission at the country level.

There needs to be a better characterization of hotspots, with more testing and new methods, for example: real time PCR to test more samples, improved diagnostics, sero-surveys...

- There needs to be more dialogue between the Health and WASH sectors on transmission routes so that WASH actors can tailor WASH interventions. It is critical to understand the main drivers of transmission routes (human-to-human vs environmentally mediated) to design an optimal WASH package and how to deliver that package.

- The successful implementation of the roadmap relies on the uptake of interventions. One of the key questions is to better define the WASH package and required coverage to interrupt cholera transmission and how to combine WASH with OCV. Combined interventions could be tested in a few hotspots to demonstrate the roadmap strategy and to help get political engagement. Even though the surveillance data will never give a perfect picture of cholera disease burden, what study designs will allow for sufficient impact credibility to be convincing?

2. Summary of cholera research questions

The implementation of *Ending Cholera Roadmap* in country has two main pillars:

- Early detection and containment of outbreaks
- Targeted multisectoral interventions for prevention in cholera hotspots

In this context and starting from the research areas identified by the GTFCC Working Groups, the group agreed that the key research questions on cholera are:

- Where is cholera and how much cholera is there? What methods of surveillance do we need to use to answer these questions?
- What are the transmission patterns? How does cholera transmit within communities, and move within countries and across borders?
- Which household/community interventions should be combined?
- What are the optimal interventions for OCV (e.g., dosing schedule, target population) and WASH (sufficient to stop cholera transmission in synergy with OCV) and how to deliver them most efficiently?
- What are the effectiveness, benefits and impact of these interventions in the short and in the long term?

3. Gaps, challenges and other considerations

The main challenges to meet the objectives of the Roadmap will be to stop transmission from cholera hotspots and related to this to stop new cholera introductions from cholera endemic areas and to contain the next explosive, unpredictable outbreaks. The group also identified key challenges and questions to consider:

- Defining the types and level of WASH needed to prevent cholera transmission
- The identification of main risk factors for cholera to define tailored approaches and packages of interventions for specific contexts
- Identifying the key determinants for behaviour change and to measure progress
- Engagement of countries and political will
- Understanding the effects of climate change on cholera
- Establishing links with other global approaches such as Universal Health Coverage, Open Defecation Free, diarrheal disease control programs, surveillance systems beyond cholera....There also needs to be more emphasis on cross-border efforts and vulnerable communities that do not benefit from national programmes
- Research and programming in restricted areas such Northern Nigeria, Yemen, Somalia
- There also needs to have more emphasis on health economics

It will be important to focus on social sciences to understand the policy drivers and enabling factors that dictates behavioural changes. A landscape analysis on the determinants for political will and engagement to ensure the sustainability of WASH services would be a good first step.

PROBLEM STATEMENT

The goal of the GTFCC research agenda is to support the implementation of the Ending Cholera Roadmap in countries through evidenced based interventions to control or eliminate cholera. More specifically, research will help target and improve multisectoral, integrated interventions, optimizing resources to be cost-effective, to sustain gains and to provide value for money.

PRIORITISATION OF RESEARCH QUESTIONS

The priority research questions have been organised by sequence, from activities occurring before the implementation of interventions to monitoring and evaluation. This is in line with countries processes and with the critical path approach. The group agreed on the following priorities:

PRE-IMPLEMENTATION	IMPLEMENTATION	POST IMPLEMENTATION / M&E
<p>BURDEN OF DISEASE AND IDENTIFICATION OF HOTSPOTS:</p> <ul style="list-style-type: none"> Description of existing hotspots to inform the definition of hotspots: <ul style="list-style-type: none"> <i>Quantification:</i> laboratory confirmation, sero-surveys <i>Characterization:</i> changing incidence and timing, WASH conditions, transmission (in and out) Accessible laboratory confirmation methods in hotspots Develop and pilot an assessment tool – hotspot vs at risk (using a tier approach), including lab capacity Improve estimates of mortality and where it occurs <p>TRANSMISSION DYNAMICS:</p> <ul style="list-style-type: none"> Macro level analysis: molecular data (e.g., basic lab confirmation data and more advanced data from whole genome sequencing),, epidemiological data Community/household level : environmental vs human to human transmission, Social science Disease modelling for short term outbreak forecast 	<p>OPTIMIZATION (INNOVATION) OF INTERVENTIONS AT THE COMMUNITY LEVEL:</p> <ul style="list-style-type: none"> RDTs Use of antibiotic (targeted prophylaxis) WASH package (short, medium and long-term) Delivery strategies for OCV including new cholera vaccines, use in “controlled temperature chain” (CTC) <p>BEHAVIOUR CHANGE</p> <p>OPERATIONAL RESEARCH ON OCV : co-administration with other vaccines, simplification of delivery</p> <p>SYNERGIES OF INTERVENTIONS: OCV and WASH</p> <p>CHOLERA AND Severe Acute Malnutrition (SAM)</p>	<p>EFFECTIVENESS OF INTERVENTIONS</p> <p>CHANGE IN ATTITUDE: Lessons learnt to be documented</p>
<ul style="list-style-type: none"> SOCIAL SCIENCES Country engagement: policy drivers, determinants and barriers Documenting success stories through case studies – to be linked to advocacy efforts IMPACT: Level of WASH coverage to stop transmission, OCV duration of protection, outcomes and process for continuous improvement, role of disease estimate modelling to support countries in defining control plans, impact of outbreak response (including OCV reactive campaigns) and endemic cholera control activities COST EFFECTIVENESS/VALUE FOR MONEY 		

QUICK WINS – SHORT TERM PRIORITIES

Based on the priority research questions, the next step was to get consensus among the group on the topics to focus on in the short term:

- Country engagement: policy drivers, determinants and barriers
- Documentation of success stories – case studies in Senegal and other countries
- Treatment of cholera in patients with SAM
- Definition of hotspots: characterization of hotspots, sero-survey, assessment tool for identification of hotspots
- Defining WASH package for cholera
- Developing a short term prediction outbreak model
- OCV use in CTC
- Impact of reactive OCV campaigns

THE ROLE OF THE GTFCC

The challenge will be to ensure the good coordination between the research agenda and the implementation of the roadmap – with clear linkages with the other components of the GTFCC (Working groups, Secretariat) whilst maintaining the capacity to integrate innovation.

During the 5th GTFCC Annual Meeting, the GTFCC members agreed on the need to adapt the governance of the GTFCC to be able to support countries in the implementation of the Roadmap². This new governance includes the creation of a Steering Committee and country support platforms to better support countries, including a Research platform to coordinate the implementation of Research and M&E.

The group provided feedback on how the GTFCC could manage a harmonized prioritized research agenda through the platform and how to keep it aligned with the implementation of the roadmap.

The Terms of Reference of the research platform should include the following:

- **Coordination of research and maintaining the link between research and the implementation of the Roadmap:** by connecting the research community, donors and most importantly countries. The GTFCC has a key role to play in articulating a clear roadmap with timelines, deliverables and sequenced research to provide evidence along the way.
- **Facilitation role:** to identify access to field for research (including laboratory), to help translate countries needs into research questions and to help incorporate innovative approaches
- **Prioritization and regular updating of the research agenda:** including linkages with Working Groups and other components of the GTFCC, with space for innovation.
- **Dissemination of results** and linkages with implementation activities and advocacy efforts
- **Developing a set of metrics for monitoring progress in cholera control:** by creating a repository for monitoring data (including epidemiologic, risk factor and governance data), SOPs for standard analyses, documenting and publicizing success stories

² Presentations are available at: <https://www.fondation-merieux.org/en/events/5th-global-task-force-on-cholera-control-annual-meeting/>

- **Incentivize and facilitate the development of research capacities in affected countries**
- **Expanding the community:** by reaching out beyond GTFCC members to new technology specialists, research experts including social scientists, private sector experts and those involved with cholera control from civil society and governments

It was flagged that the coordination of all these activities will be challenging and require strong capacity within the Secretariat – with a specific function on the research agenda to maintain alignment.

BARRIERS, CHALLENGES AND MITIGATION MEASURES

Key obstacles and challenges in implementing the GTFCC research agenda were also discussed:

- **Lack of funding for activities and for the coordination mechanism:**
Mitigation: There needs to be a clear narrative and a clear list of priorities and expected impact to be communicated to donors, with continued advocacy efforts to put cholera as a priority. The GTFCC should also explore co-funding opportunities to broaden the base of donors and also engage the private sector (looking at Corporate Social Responsibility)
- **Lack of capacity to agree on an agenda and to get consensus on priorities**
Mitigation: there should be a coordinating body including Working Group representatives, countries and donors. It would also be important to develop some guidance to researchers to communicate on the priorities, with clear linkages to the Roadmap. The agenda needs to be adaptable and dynamic, and communication on this well managed.
- **Obstacles linked to countries and partners buy in:** including partners not sharing information or results (or waiting for peer review before presenting results leading to delays), and countries not engaging
Mitigation: this is also linked to the legitimacy of the GTFCC to coordinate cholera research. Communication and dissemination of success stories will help get buy in. It will also help in showing the mobilisation of resources (financial and HR). The GTFCC could plan a “roadshow” to promote the role of the Task Force to broader research groups.
- **Capacity to implement research** including lack of capacity in countries, lack of sites in Africa, difficult settings for research.
Mitigation: First there should be a mapping of potential partners based in country, especially in Africa. Another option would be to invest in a research centre in Africa able to assist other countries and able to provide support on the ground. The GTFCC research agenda should also build on existing networks (such as FETP) and should involve countries representatives to have a sustainable engagement
- **How to measure progress :** ensure there are measurable outcomes, also considering the time sequence for research can be quite different from implementation timeline
Mitigation: Research activities need to have SMART objectives and clear criteria to have measurable outcomes. There should also be opportunities for review of ongoing

activities (rather than waiting for completion/publication). A reporting schedule with interim successes would help measure progress along the way. There should also be regular meetings with researchers to provide updates on progress.

- **Expanding beyond the GTFCC network:** Failure to take advantage of opportunities coming from other spheres.

Mitigation: *The GTFCC should consider organising an annual scientific conference on cholera to communicate on activities in Africa or Asia. There also needs to be sufficient HR capacity focusing on research at the GTFCC Secretariat to manage these efforts.*

WRAP UP AND NEXT STEPS

Next steps will be to give visibility to the GTFCC research agenda and to engage donors including those previously engaged in the creation of the OCV stockpile.

The GTFCC Secretariat will follow up on the proposed research objectives and identified priorities to communicate to all GTFCC members and to countries representatives.

Annex 1. Agenda and List of Participants

Monday 23rd July 2018

9:00	Closed session: Working Group Leads
10:00	Introduction
10:20	Laying the Foundations (definition and value of research, considerations for prioritisation)
11:00	Coffee and tea
11:10	Research agenda by working group
12:10	Lunch
12:50	What are the questions we are addressing across each research agenda?
13:50	Gaps, dependencies and interplays
14:40	Prioritisation of research questions
17:30	Closing remarks for day 1 (Chair and WG Leads)
6:30	Dinner

Tuesday 24th July 2018

09:00	Research agenda: agreeing the list
10:30	Tea and coffee
11:00	Role of GTFCC in research
12:00	Quick wins
12:20	Lunch
13:20	What are the barriers to achieving our goals?
14:00	How do we overcome the barriers?
14:30	Summary and next steps (Chair and WG Leads)
15:00	Closed session: Working Group Leads Closed session: Funders
16:00	End

List of Participants

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