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Report of First Meeting of the Global Task Force for Cholera Control

26-27 June 2014

Chavannes-de-Bogis, Switzerland

World Health Organization

Acknowledgements

This report of the first meeting of the Global Task Force on Cholera Control (GTFCC) was compiled by the Control of Epidemic Diseases (CED) Unit in the Department of Pandemic and Epidemic Diseases (PED) at WHO/HQ.

We wish to thank all our partners including other UN agencies, research institutions, universities, government and nongovernmental organizations (NGOs), donors, representatives of health ministries for attending this meeting and for providing technical input and comments to the report. A full list of participants is attached in Annex 2. CED also wishes to thank the collaboration and input of numerous experts within WHO, who are also listed in Annex 2.

Professor David Sack, Department of International Health, John Hopkins University Bloomberg School of Public Health deserves a special mention, for chairing the meeting and for his tireless input on Cholera Control.

Mr Kai Lashley is gratefully acknowledged for writing and editing this report.

Contents

Abbreviations and acronyms

CDC	(United States) Centers for Disease Control and Prevention
CFR	Case Fatality Rate
CTC	Cholera Treatment Centre
CTU	Cholera Treatment Unit
DOVE	Delivering Oral cholera Vaccines Effectively
FCR	Free Chlorine Residual
GAVI	Global Alliance for Vaccines and Immunization
GOARN	The Global Outbreak Alert and Response Network
GMP	Good Manufacturing Practices
GPHIN	Global Public Health Information Network
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GTFCC	Global Task Force for Cholera Control
HWTS	Household Water Treatment and Safe Storage
ICCM	Integrated Community Case Management
ICDDR'B	International Centre for Diarrhoeal Disease Research, Bangladesh
IDSR	Integrated Disease Surveillance and Response
IFRC	International Federation of Red Cross and Red Crescent Societies
OCV	Oral Cholera Vaccine
MSF	Médecins Sans Frontières
NGO	Nongovernmental organization
PHAST	Participatory Hygiene and Sanitation Transformation
SAGE	Strategic Advisory Group of Experts (on Immunization)
SMS	Short Message Service
UNICEF	United Nations Children's Fund
WASH	Water, Sanitation and Hygiene
WER	Weekly Epidemiological Record
WHO	World Health Organization

Introduction and background

Cholera is a preventable and treatable disease that today still kills over 100 000 people each year; and its disease burden affects over 1 billion[1], particularly vulnerable populations (e.g. people living without adequate access to water and sanitation, or those affected by conflict and natural disasters). Though there is knowledge on how to prevent and treat cholera, the disease continues to burden societies.

The 2011 World Health Assembly resolution WHA64.15 ("Cholera: mechanism for control and prevention") requested the World Health Organization (WHO) Director-General to revitalize the Global Task Force for Cholera Control (GTFCC) and to strengthen WHO's work in this area, including improved collaboration and coordination among relevant WHO departments and other stakeholders. To that end the GTFCC was revitalized through a process begun in December 2012 and completed in early 2014. Terms of reference have been agreed upon (see Annex 1). The first meeting of the revitalized GTFCC – on which this text reports – was held in June 2014 to finalize membership and priorities.

The meeting was chaired by Professor David Sack. In line with WHO policy, all external participants had completed and signed Declarations of Interest forms in advance of the GTFCC meeting which had then been reviewed by the WHO secretariat in consultation with the WHO Legal Office. Upon review, it was concluded that in light of the scope of the work to be undertaken, none of the interests that were declared by participants was considered to represent any conflict of sufficient significance to warrant exclusion of any expert from contributing to any part of the discussions.

It was noted during the opening of the meeting that cholera is a complex public health problem requiring cross-sectoral solutions and broad stakeholder collaboration. WHO convened the first meeting of the GTFCC to identify those solutions, bring together partners also committed to cholera control (Annex 2 lists the participants of the meeting) and set a research agenda to better coordinate stakeholder efforts.

The Global Task Force for Cholera Control

History (Alan Hinman)

In response to the cholera outbreak in Haiti and in parts of Africa in 2011, WHO decided that resources to combat the disease needed to be bolstered, which included the Global Task Force for Cholera Control (GTFCC) that was originally established in 1991. The 2011 World Health Assembly resolution WHA64.15 requested the WHO Director-General to

[1] Given the rapidity with which the disease can lead to death, and that populations affected are often living in low-resource settings where cases are underreported, the actual disease burden is likely to be higher than what is officially reported.

strengthen WHO's work in the area of cholera control among stakeholders and relevant WHO departments, including the revitalization of the GTFCC.

The Bill & Melinda Gates Foundation provided a grant to the Task Force For Global Health to work with WHO to undertake the revitalization of cholera control efforts worldwide, through the GTFCC. Ten colleagues from both organizations initiated the revitalization process in February 2013, holding working group meetings in March and September 2013[2] to define the stakeholders to be involved and broadly, the structure of the GTFCC (e.g. strategy, goals, coordination, membership, etc.). Working group members also solicited feedback from a wide variety of actors in the field of cholera control through a formal stakeholder analysis.

The main responses about strategy included the following actions: coordination of all stakeholders, resource mobilization and advocacy for an integrated approach to cholera control. This involves:

- design and implementation of a global strategy;
- development of norms and guidelines in accordance with WHO standards, which follows the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach;
- mobilizing technical resources to strengthen country capacity;
- facilitating implementation and monitoring of evidence-based interventions at the country level;
- facilitating advocacy and resource mobilization activities;
- serving as a global platform for integrating and disseminating data and knowledge;
- developing and supporting a research agenda for cholera prevention and control;
- encouraging innovative approaches to cholera control in affected countries;
- effective implementation of water, sanitation and hygiene (WASH) interventions;
- wider use of oral cholera vaccines (where appropriate);
- advocacy for an integrated approach to cholera control.

It was decided during these meetings that the GTFCC should comprise 10 to 15 members, a mix of institutional and individual representation, with a staggered rotation. WHO would serve as the Secretariat, and voluntary working groups would carry out the work of the GTFCC. The final terms of reference were decided on 23 April 2014.

Status of the GTFCC and its terms of reference (Anais Legand)

Following resolution WHA64.15, stakeholders within WHO discussed the status of the revitalized task force to define its role both outside and within WHO. They decided to make the GTFCC a network, which means the task force will be relatively nimble and have the capacity to respond quickly to developments in cholera outbreaks and epidemics. Such status was the best fit for the vision and aim expressed by the Department of

[2] Detailed reports of the stakeholder meetings can be found at: http://www.who.int/cholera/task_force/Revitalization/en/.

Pandemic and Epidemic Diseases (PED) of WHO as well as WHO's general operating procedures: stopping cholera transmission and ending cholera deaths through strengthened international collaboration and increased coordination of partners. Networks do not need to report to the Executive Board (unlike the Strategic Advisory Group of Experts, SAGE).

The GTFCC will not be a body proposing official guidelines (though its work may lead WHO to update guidelines and recommendations such as the 1993 Cholera Guidelines), nor will it be a legal entity. GTFCC will follow WHO's rules and regulations and be administered by WHO (see Annex 1). It will act instead as a flexible mechanism of collaboration among stakeholders, aiding the effective implementation of evidence-based research to reduce cholera's disease burden.

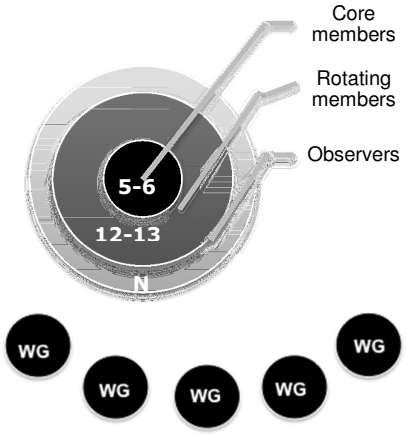
The complete terms of reference of the GTFCC are detailed in Annex 1.

Management of the GTFCC: composition and scope (William Perea)

Membership

Discussion during the meeting led to the following structure of the GTFCC: the task force will comprise 5-6 core members, 12-13 rotating members and a number of observers to be determined (see Figure 1). A pre-requisite for inclusion will be that the members be institutions working in the area of cholera control. Exclusion criteria include the following: for-profit groups, conflicts of interest, and absence from two consecutive meetings. Membership in the GTFCC will be voluntary and comprise representatives from different institutions.

Figure 1. Composition of the GTFCC



Suggestions for core members included the United Nations Children's Fund (UNICEF), International Federation of Red Cross and Red Crescent Societies (IFRC), Médecins Sans Frontières (MSF), International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR'B), Centers of Disease Control and Prevention (CDC) and WHO. WHO will also act as the Secretariat. Rotating members are to include institutions, university

initiatives, nongovernmental organizations (NGOs), representatives of health ministries, etc. that are involved in cholera control and express interest in participating, subject to approval from the GTFCC. Rotating members would round off membership with a 'contract' of 2 to 3 years renewable; they would leave and join in a staggered fashion. Observers would include donors.

Functions

Discussion clarified the desires of the meeting participants on the details of the GTFCC leadership and functions. The chairperson would be an active leader and 'ambassador' for cholera control, an expert on the subject, and a member of the GTFCC. A vice-chairperson would assist, have a different background from the chairperson, and ascend to chairperson after the original person retired from the role after 3 years (to ensure continuity of focus).

Meetings will be held twice a year, with the first three occurring in a central location to facilitate a solid formation of the group. Thereafter there should be at least one face-to-face meeting per year. The GTFCC will endorse (or modify) each working group's recommendations, with consensus being used for the decision-making process. A quorum of at least half of the institutions of the GTFCC should be represented (by their representative or his/her substitute) for decisions to be made.

The GTFCC will develop a monitoring and evaluation framework (outputs, outcomes and impact indicators) and communicate its activities via:

- web-site with regular updates of GTFCC/working group activities;
- outcomes of the meeting published in the Weekly Epidemiological Record (WER);
- diffusion of technical documents/guidance by the Secretariat (posted to the GTFCC web-site and given to GTFCC members).

Working groups

It was decided that the working groups will cover five domains.

1. Surveillance/Epidemiology
2. Oral cholera vaccines (OCVs)
3. Case management
4. Water, sanitation and hygiene (WASH)
5. Communication/social mobilization

The work in each domain will be undertaken by working groups of approximately 6-8 members who may or may not belong to the GTFCC. Working groups will be created on an ad hoc basis for each domain with defined objectives.

Working groups will:

- address priority issues in each domain;
- identify/invite individual experts as required;

- nominate a leader who will head the working group and be the liaison with the GTFCC. The leader of each Working Group will be a member of GTFCC;
- meet virtually and face-to-face for discussion;
- report results/recommendations to the GTFCC.

Time frame

Mid-August: Expression of interest form sent to all participants responding to the invitation of the 1st meeting and any other stakeholders interested who were not able to attend the 1st meeting.

Mid-September: Expression of interest submitted with designated focal point and back-up person.

End September–early October: Selection and formal establishment of the GTFCC, development of the working groups' terms of reference and their formal establishment.

Quarter 4: First meetings of the working groups.

Methods for cholera control: situation analysis and priorities for action

Presentations on day two focused on six domains considered vital to prevention and control efforts of cholera. Discussions presented each domain's current focus, challenges and priorities for action. A presentation on cholera prevalence in the WHO regions began the day.

Introduction: cholera prevalence in the WHO regions (WHO ROs)

Cholera's disease burden weighs most heavily on the Regions of Africa and South-East Asia. Between 2004 and 2013 the African Region reported between 10 000 and 250 000 cases; fatalities occurring from cholera infection were greater than 5% in many countries. The actual number of cases is considered to be much higher because of under-reporting.

In many instances in the African Region, cholera is not imported but reoccurs regularly in particular areas or districts, both urban and rural. Such areas are considered 'hot spots' for cholera transmission. They are characterized by frequency of occurrence, persistence of reported cases during a 'lull' period and a high attack rate. The number of people living in hot spot areas in the region is almost 44 million (~12.5% of the population of the most affected countries and 4% of the Region's total population).

Identifying cholera hot spots requires at least 3 years of historical case data (ideally 10 years). Hot spots were defined according to the number of years with cases reported (at least 3 years) and attack rates over the period (>0.1%). In some instances there are sufficient data to identify the hot spots (e.g. in the Democratic Republic of the Congo) while in others data are limited (e.g. Nigeria). Given that hot spots may be the starting point for larger epidemics, evidence-based data from these areas is required – not only to tailor responses in the hot spots, but also in service to cholera control globally. This begins with enhanced surveillance in those settings, working with actors also outside the health sector (silo approaches do not work), and incorporating subregional approaches (e.g. West African coast, lake Chad region).

The cholera situation in the Region of the Americas was also discussed. Between 1991 and 1996, South America had over 1.2 million cases (>12 000 fatalities) from the cholera strain introduced in 1991 (which importantly, did not affect the Caribbean). By 2000, the number of cholera cases in the Region was decreasing, until 2010 when a cholera strain different from that of 1991 was introduced in Haiti. The cholera outbreak in September of that year has led so far to over 700 000 cases (the early CFR was approximately 9–10%, and has since been reduced). Within a month, the first cases were reported in the Dominican Republic and by July 2012 cholera had spread to Cuba, initially in an area of the country with high levels of poverty and less access to water and sanitation.

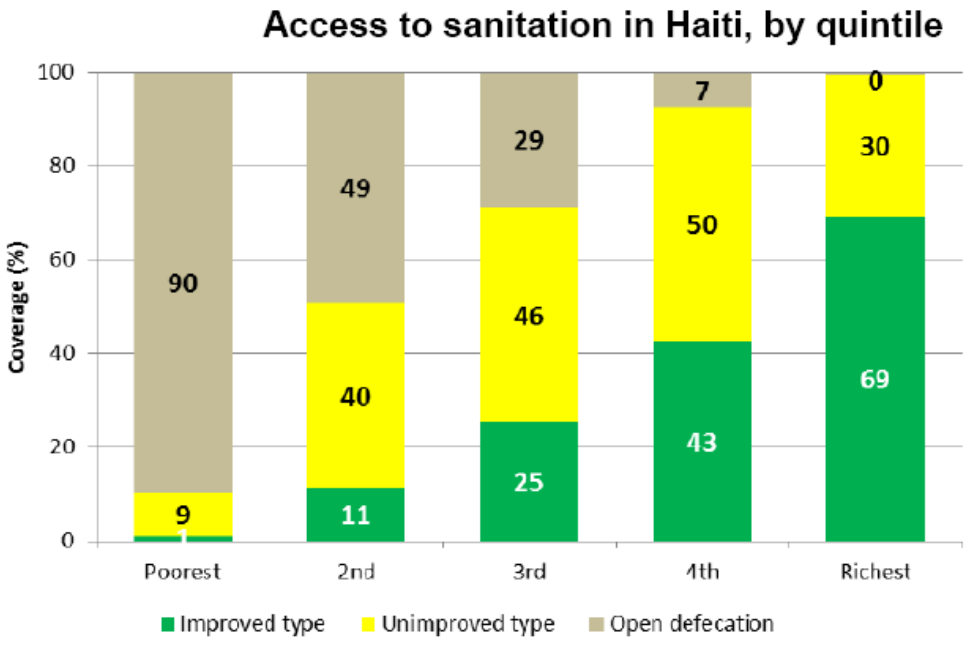
In September 2013 cholera was reported in the greater metropolitan area of Mexico City, during random sampling of diarrhoeal cases. Having reached the mainland, the concern now is that cholera will spread south through Central America; there are large populations of indigenous and rural people, who do not speak Spanish (meaning they are not reached by normal messaging) and cannot or do not access health centres. An outbreak among these populations likely would mean excellent conditions for cholera transmission and numerous fatalities.

Case reporting in countries affected by the current cholera outbreak is generally good, but could be better. In Haiti, for example, several districts are either not reporting data or have no functioning structure in place to deal with cholera—itself a form of data providing health workers with probable hot spots in the country. Data from the Dominican Republic over the course of the outbreak indicate lapses in cholera control. Initially the health system dealt effectively with the outbreak, but in 2011 during the rainy season when the water infrastructure was inundated and non-functioning, there was a spike in cases and fatalities.

This underscores the link between cholera transmission and sanitation and access to safe water, which is also shown in Figure 2. Moving from a project approach to a programme approach was stressed with improvement in the WaSH situation in Haiti key to controlling cholera – the silo approach has been found to be less effective than an integrated one.

Bridging environmental surveillance with epidemiological surveillance is also essential.

Figure 2. Access to sanitation in Haiti, by wealth quintile



Source: UNICEF, *Call for Action for WASH investment* (2012).

Epidemiology (Eric Mintz)

Epidemiology is a valuable tool for making predictions about the future. In the context of cholera, it is especially valuable to be able to predict whether or not an outbreak will occur, and how fast and how far it might expand if it does. Accurate predictions can inform wise use of resources, including OCVs.

Surveillance and disease prevention programmes go hand-in-hand; one is pointless without the other. Surveillance relies on reporting, which in turn relies upon an accurate case definition. In the cholera epidemic in Haiti, for example, different definitions of cholera were used, which affected reporting. Similarly, case fatality rate (CFR) can be interpreted differently, as can definitions of 'endemic' and 'epidemic'. Such discrepancies in definitions can and do result in underreporting of cholera cases, which is a large problem in terms of treating cholera and targeting resources. Standardization, therefore, should be one of the main goals of the GTFCC.

A number of considerations are required to develop an epidemiologic research agenda for cholera, particularly: defining cholera, reviewing its emergence and transmission, and working towards prevention and control (i.e. What epidemiologic evidence is needed to inform more effective prevention and control efforts?).

In some areas of cholera control, data inform prevention and treatment, while in others, conventional wisdom is relied upon. It was suggested that all epidemiological data be reviewed and re-analysed in light of new technologies to definitively answer questions about disease vectors. Cholera carriers are a good example: historically, carriers' role in disease transmission has been considered negligible. Tools available today could definitively inform this question, ensuring that the information for cholera control is evidence-based. Other such questions include the following:

- What is the role of *V. cholerae* persistence in the environment? Whole genome sequencing is one of the tools that may help answer this question. And if this vector is important, how will this knowledge improve prevention and response strategies?
- Can changes in the environment help control the disease? (It was noted that the removal of vast blooms of water hyacinth from Lake Victoria in Kenya was followed by a long period of cholera quiescence in the populations who live along its shores.)
- In what situations is antimicrobial chemoprophylaxis or mass treatment useful? While some guidelines recommend chemoprophylaxis and mass treatment for special situations where a cholera outbreak occurs in a forcibly closed population (e.g. prisons), there appear to be no such guidelines that address cholera control in live-in institutions such as military barracks, boarding schools or orphanages. There are also no guidelines on how to implement potentially life-saving chemoprophylaxis or mass treatment in prisons or other incarcerated populations, and no recommendations about other measures that should be taken alongside the chemoprophylaxis in these institutions.

Variables that affect cholera outbreaks and expansion include: access to safe water – two thirds of countries where populations have >70% access to improved source of water will have lower cholera endemicity; shared sanitation with more than five families appears to be a risk factor for diarrhoeal diseases, including cholera; living near open landfills and sewers may be a risk factor as well. Basic food hygiene is also one of the key issues to be taken into account.

The questions above are not exhaustive. The presenter suggested the audience members come forward with other questions about which they would like more information on epidemiology to improve cholera prevention and control.

Water, sanitation and hygiene (Daniele Lantagne)

Water, sanitation and hygiene (WASH) interventions play an important role in cholera control efforts.

The overarching long-term goal for safe water supply is the provision of piped, treated water in an infrastructure system. Where properly managed, the advantages of infrastructure include the consistent provision of reliable, high-quality water, which reduces the incidence of waterborne disease; increased free time (that can used for other pursuits); and hygiene promotion (e.g. increased hand washing). Such infrastructure has significant costs, however, including initial and on-going financial investment and use of energy to power the system. It also requires political stability.

In the absence of water supply infrastructure, various methods are used to prevent the spread of cholera and other diarrhoeal diseases. Unfortunately, there is a lack of data for many of these interventions, or inconsistent recommendations on their use. Adding chlorine to a particular quantity of water, for example, can be effective, but there is no standard on how to dose (e.g. there are inconsistent free chlorine residual recommendations); the dose is critical to inactivate most of the bacteria and viruses that cause diarrhoeal diseases.

Chlorination options currently used with few data on efficacy include bucket chlorination and use of tanker trucks. Data show that neither well chlorination nor pot chlorination are effective in treating water in the medium- to long-term, but both interventions are still used. Where there are data showing efficacy (chlorine dispensers for example), reductions in waterborne disease are linked to uptake of the intervention – if it is used, it works – meaning that education and social outreach about the issue must accompany the intervention.

While an intervention may be efficacious, it is not effective unless it is implemented correctly. Data show that paying workers to disseminate information to communities leads to broader uptake of WASH programmes, particularly within the context of adequate chains of supplies, proper implementation of the intervention, trained staff, integration within the larger WASH programme, etc. Data show that

uptake of an intervention can vary between 3% and 96%, based on how well that intervention is implemented.

There is very little research on sanitation in emergencies. Building latrines as fast as possible is the current approach, though there are a few studies looking at how to treat the waste coming from cholera treatment centres, so it does not re-enter the environment and re-infect people.

There are no data on the efficacy of chlorine spraying of homes to reduce disease. Despite this, the activity (a perceived wisdom that provides the illusion of a concrete action) is routinely undertaken, which is another reason to conduct studies on efficacy and collate existing research on this and other WASH interventions.

It is known that emergency response teams employ more or less the same methods in each emergency. The challenge is getting context-specific data to these teams (and their organizations) so they can tailor approaches to emergencies. This, then, is a possible area in which the GTFCC can lead – by providing a guidance document on such tailored approaches and harnessing institutional 'buy-in'.

Surveillance (Martin Mengel)

There are three major processes involved in surveillance: collection of data, its analysis and dissemination. Surveillance and epidemiology are linked; as was discussed above, surveillance is ineffective without a control programme to act the data garnered. The discussion on surveillance, however, showed the problems with the data: for example, the differing definitions of suspected cases and confirmed cases set by WHO, Integrated Disease Surveillance and Response (IDSR) and individual countries. This of course leads to data limitations, but the problem extends further: to discrepancies in reported (300 000–500 000) and estimated cases (2.5 million and 2.8 million) of cholera.

Such discrepancies of course stem from the different case definitions, but also from the fact that all surveillance currently is facility based; there is no community surveillance. With only 3–5% of cases culture confirmed, it is clear that the data are not reflecting the actual disease burden of cholera, particularly in children aged less than 5 years.

Modelling can bridge data gaps with quick approximations (e.g. by providing helpful estimates on the herd protection conveyed by currently available vaccines).

Surveillance systems

Both IDSR and sentinel systems like Africhol have advantages and disadvantages. For example, data aggregation in IDSR is important (going from the local CTCs to the district, province and the health ministry) while it is less in sentinel systems (which only provide case-based surveillance such as household and environmental data). Case-based surveillance allows for granularity of data, for example in pinpointing certain areas as the centre of an outbreak or hot spot, and allows for the description of epidemic and endemic areas (which help decision-makers to prioritize

sanitation and water access interventions in target areas, for example). While IDSR data are often rudimentary, they do allow for the study of spatial and temporal disease spread. In many ways the disadvantages of one system are made up by the advantages of the other, which is why surveillance systems should ideally work together.

Laboratory

Culture confirmation is the gold standard in accurately identifying *Vibrio* species. Such confirmation requires time (specimens must be sent for testing), which makes rapid diagnostic tests (RDTs) an attractive option, particularly in low-capacity settings. However, at approximately US$ 1.5 current rapid tests are too expensive for governments of low-income countries and require specialized training to use. Further, there are some issues related to quality control, quality assurance and supply chain, which are also barriers to use of current RDTs.

Cheaper, easier to use RDTs are under development (e.g. Columbia University is developing one based on yeast that changes colour when in contact with *Vibrio*). Molecular diagnostics are also being used to elucidate the origin and spread of outbreaks.

Oral cholera vaccines (Balakrish Nair)

Evidence has shown that use of OCVs can reduce cholera's burden of disease. For example, a large randomized, placebo controlled trial in a rural Bangladeshi population with endemic cholera demonstrated that the Dukoral vaccine conferred 85% protection against cholera for 4 to 6 months after dosing; the protection declined to 62% at one year and 57% during the second year.[3] Recent data from a study in Kolkata, India, showed cumulative protective efficacy was 65% at five years[4].

Given the clinical study results on OCVs, WHO and partners decided to create an OCV stockpile for outbreak response and use during humanitarian crises to reduce the risk of cholera. There are three OCVs currently licensed. Figure 3 compares the two most widely used, Dukoral™ and Shanchol™.

[3] Clemens JD, Sack DA, Harris JR, Van Loon F, Chakraborty J, Ahmed F, et al. Field trial of oral cholera vaccines in Bangladesh: results from three-year follow-up. Lancet. 1990;335:270–73.
[4] Sujit K Bhattacharya et al. 5 year efficacy of a bivalent killed whole-cell oral cholera vaccine in Kolkata, India: a cluster-randomised, double-blind, placebo-controlled trial. Lancet Infect Dis 2013; 13: 1050–56.

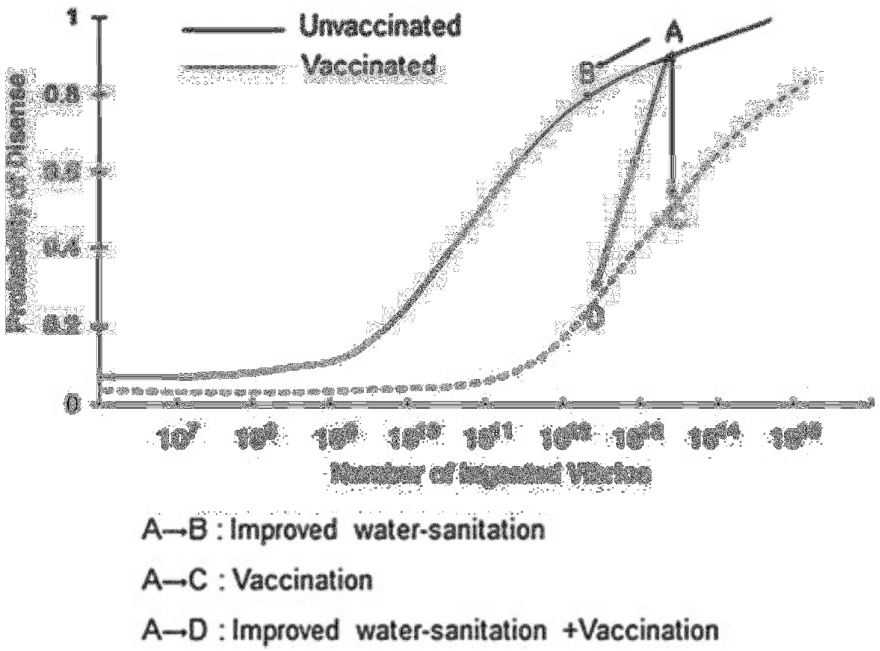
Figure 3. Comparison of currently manufactured WHO prequalified OCVs

	Shanchol™	Dukoral™
Contents	Killed whole cells of *V. cholerae* serogroups O1 and O139	Killed whole cells of *V. cholerae* serogroup O1 and recombinant B-subunit of cholera toxin
Recommended age	≥1 year old	≥2 years old
Recommended dosage	2 doses, 2 weeks apart for all age groups[a]	2–6 years old: 3 doses 1–6 weeks apart each dose >6 years old: 2 doses 1–6 weeks apart[a] Booster every 2 years
Buffer requirement[b]	None	2-6 years old: Buffer dissolved in 75 mL of water >6 years old: Buffer dissolved in 150 mL of water
Efficacy[c]	65% after 5 years for >5 year olds; 43% after 5 years for 1–5 year olds	85% after 4–6 mo.; 57% after 2 years for >6 year olds; 0% after 2 years for 2–6 year olds
Duration of protection[c]	At least 5 years	2 years
Cost[d]	$1.85/dose	$5/dose

a. Two week interval between doses is recommended, but the interval can be longer if logistically necessary.
b. Buffer is needed for Dukoral™ because the B-subunit is acid sensitive and will likely be inactivated if given without buffer.
c. Efficacy rates are from double-blind placebo-controlled trials; however, the whole cell components of the two vaccines are similar, and the duration of protection may not differ significantly.
d. Cost listed is the cost for purchase through the UN system. Cost of Dukoral™ in the private market is higher.

An important aspect of the effectiveness of OCVs in control of cholera outbreaks is their potential to synergize with concomitant WASH interventions to prevent cholera. Figure 4 shows a potential synergy.

Figure 4. Hypothetical relationship between impact of OCV and WASH on the risk of cholera transmission



Source: Clemens J and Holmgren J. When, how and where can Oral Cholera Vaccines be used to interrupt cholera outbreaks. Current Topics in Microbiology and Immunology (2014) 379:231-258.

The top curve corresponds to an unvaccinated individual and bottom curve to a vaccinated individual. The top curve roughly describes the lower risk of symptomatic cholera after WASH interventions, which act to decrease the frequency and/or dose of ingestion of cholera (movement state A to B).

The bottom curve reflects the same for vaccinated individuals (movement from state C to state D). The effect of OCVs should be to decrease the probability of becoming ill, at any (or at least most) ingested doses (movement from state A to state C). Because of these relationships the combined effects of WASH intervention and OCVs should produce a greater preventive effect than either intervention alone (movement from state A to state D).

Costs of the vaccines are a factor in use. While Shanchol™ is less expensive than Dukoral™, its cost (approximately US$ 3.00 per dose, after delivery and operational costs are added) could still be a barrier for health systems in developing countries compared to other measures in cholera control. OCVs can be considered cost-effective, however, when used strategically, for example within the 'continuum of care' of cholera control.

Research on single-dose OCVs is under way. A collaborative double blind, placebo-controlled study is being conducted by the International Vaccine Institute (IVI) and ICDDR,B. Such treatment could potentially lower the cost and logistical requirements of OCVs drastically.

Case management (Myriam Henkens)

Proper management of cholera refers to correcting or preventing dehydration with the appropriate quality and quantity of fluids as rapidly as possible after symptoms present. It also encompasses complementary therapies (e.g. antibiotics, zinc) to reduce the duration and severity of diarrhoea, with the goal of resuming normal eating as soon as possible, especially in children. Complications include hypoglycaemia and hypokalaemia.

While standard treatment includes oral rehydration salts, there are some questions remaining about the complementary therapies of antibiotics and zinc administration. In the former, the most severe patients would receive antibiotics, with the preference being for a single-dose treatment. In the latter, all children aged under 5 years would receive such a treatment, though there have been some calls for treatment of children up to the age of 15 as well. Finally, there is no definitive guideline for treatment of special cases, such as pregnant women, the elderly and those with co-morbidities like malnutrition.

Generally speaking, treatment is organised to three levels: the cholera treatment centre (CTC), cholera treatment unit (CTU) and oral rehydration salts (ORS) point; at the latter level a system flags serious cases for referral for treatment at a higher level of care. Quality of care focuses on:

- standardized protocols and correct implementation;
- specific training, coaching;
- adequate supervision;
- adequate and rapid supply (of Ringer's Lactate or ORS for example);
- management of stock;
- systematic review of all deaths and all major complications to improve care delivery.

Organization of the three levels is fairly straightforward in urban settings/refugee camps. In rural settings where access to health facilities is limited, the formula is less clear. The goal is to establish multiple CTU/ORS points with referral, with the addition of mobile teams that can assess the local situation, assist with setting up CTU/ORS points, provide training, supervision, surveillance, resupply, etc. In certain cases ORS points are set up along a main road leading to the CTU, or ORS are distributed to homes in affected areas.

Questions remain about the best model of care in rural areas to decrease CFR. For example, what does 'close to patients' actually mean in terms of distance and travel time? What is the trade-off between proximity of care and quality of care (staff with limited training, limited supervision, etc.)?

And how effective are the strategies of ORS distribution: in communities and homes and at ORS points without referral possibilities (ambulance systems)?

Implementation issues remain as well. Which data (and how) should be collected, analysed and used for improving response (i.e. to decrease CFR) and modifying the intervention when necessary? What is needed in terms of training, coaching, support and supervision?

Social mobilization (Kate Alberti)

Mobilizing the public is a critical part of the continuum of care mentioned above. Most behaviours are not inherent in humans; they are learnt. But when disseminating information (about WASH interventions, for example) the information or message needs to be targeted effectively. The three main points to consider are: right channel, right message, right audience, all of which help to overcome barriers to uptake.

Informing the public about issues is ultimately about the individual, but appropriate messages must also reach and enrol interpersonal networks (family and friends), organizations and communities (e.g. places of worship and religious leaders, traditional healers, midwives), as well as informing public policy through the enactment of national, subnational and local laws.

It is not enough to disseminate messages; their impact and associated campaigns must be monitored, evaluated and adjusted when necessary (e.g. after input from community members), which is done in some settings. There are other areas where effectiveness can be improved.

- Increase the evidence base of interventions.
- Ensure better collaboration and utilization of community resources.
- Become more flexible in anticipating when changing an approach is necessary (including adjusting one-way communication to two-way communication).
- Communicate to all levels of the population including health staff, government, etc.
- Consider the impact of fear and stigma on the intervention.

Technological innovation is leading to improved assessment methods. Since mobile phone penetration in developing countries is high, use of phone technologies can assist in information dissemination, for example mobile phone surveys and health messages via Short Message Service (SMS).

Approaches to mobilization are not being tailored to cholera outbreaks from general cholera control. Gaps in supplies like soap also raise the issue of sustainability: interventions are often short-term solutions for (in some cases) long-term problems (e.g. hot spots).

Synergy versus silo approach

Opportunities expand with coordination and collaboration. There is no reason why approaches like participatory hygiene and sanitation

transformation (PHAST), social marketing and community-led total sanitation cannot be integrated. Similarly, work can and should involve different sectors. For example, integrated community case management (ICCM) is a strategy for reducing mortality among children in developing countries, particularly where access to health facilities is limited. Community health workers are trained in basic methods to treat several diseases, given supplies and evaluated over time. Evidence on this intervention is proving it is effective.

Why not work also with Guinea Worm prevention programmes, or piggyback oral cholera vaccines on the cold chain infrastructure that polio programmes have implemented with great success? Such synergy will also mean less financial outlays (limiting a big threat to sustainability) of interventions.

Working groups: Priority areas for the GTFCC over the next year

The meeting participants were divided into groups covering the six fields discussed above. Experts in respective fields were mixed in each group to ensure that discussion of a particular field (e.g. OCVs) also contained experts from other fields (e.g. case management). Participants were asked to define a list of actionable tasks to assign to the working groups, in particular three that would be achievable within 12 months. A summary of their work is below.

It was suggested during the group work that the working groups on epidemiology and surveillance be joined; there is much overlap in these domains and combining them will reduce workload.

Epidemiology

Priorities for the first year of the GTFCC are shown below.

1. Clarify and standardize terminology, among others the terms 'endemic', 'epidemic' and 'hot spot'. GAVI was given as an example of an organization that replaced the first two terms with 'expected' and 'unexpected' outbreaks, respectively, to better define areas affected by cholera; this might be considered for use by the GTFCC.
2. Contribute to revised cholera guidelines through strengthened protocols for investigations and case factors (death/case ratio, outbreak confirmation as well as monitoring and evaluation of various interventions like WASH).
3. Create data collection tools and platforms for sharing data (e.g. smartphones, databases, repositories), looking particularly at such tools and expertise in other disease control contexts (e.g. HIV, TB), which the GTFCC could tap to increase its knowledge base at the local level.

Research agenda

4. Define the predictors of epidemic resurgence/emergence.
5. Gather additional data so interventions (OCVs, WASH) can be better targeted: for example WASH coverage by district, demographics by district and epidemiological week, and behaviours that could both assist and hinder interventions.
6. Determine what is known and where there are gaps in geospatial and temporal aspects of cholera.

Water, sanitation and hygiene

Priorities for the first year of the GTFCC are shown below.

- Review evidence of recommended WASH practices, particularly: sanitation, with regards to: outbreak response; efficacy, effectiveness, feasibility, community perception and cost; research needed; (grey) literature review; new technologies.
  Output: Publish and disseminate a report of the review.

- Integrate WASH with other control strategies: review best practices to be able to integrate with programmes on malaria, neglected tropical diseases, and other vaccination campaigns; set up pilot projects.
  Output: Summarize the current experiences on integrated strategies and recommend pilot projects (grant proposal).
- Investment case for WASH interventions in hot spots.
  Output: Investment case report.

Research agenda

- List of current practices and literature review is urgently needed to establish priorities.
- Monitoring and evaluation activities of integrated strategies should be planned as quickly as possible.

Further potential working group questions

Research priorities: most cost-effective sanitation practices, hygiene promotion (social and anthropological aspects among others), the potential role of water filtration (versus chlorination, which does not affect cryptosporidium, giardia), free chlorine residual practices, use of 'perceived wisdom' (doing what had worked in the past) rather than evidence- based approaches (from specific studies or programme implementation) which provide data about efficacy or effectiveness of interventions.

Surveillance

Priorities for the first year of the GTFCC are shown below.

1. Compile existing data: develop a plan on how to gather and unify data from different sources, the goal being more granular data being disseminated more frequently than once a year in single location.
2. Revise cholera case definition and develop a plan to advocate for its diffusion at the country level. This would contribute to the new cholera guidelines being developed by the GTFCC.
3. Foster subregional collaboration on surveillance and response, vis-à-vis highly endemic areas (e.g. central Africa).

Research agenda and longer-term goals

- Assess technical innovations for surveillance (e.g. GPHIN, Webcrawler, smartphone applications) and real-time notifications (e.g. Google flu tracker): benchmark these existing products/tools and their applicability to cholera.
- Bridge surveillance with other disease programmes (e.g. malaria, polio).
- Integrate community-based reporting (e.g. SMS and Twitter feeds from the general public, auxiliary health workers, etc.) within cholera surveillance systems.
- Integrate laboratory confirmation and results as a routine (standardized) parameter to be reported (e.g. the CDC's PulseNet).

It was envisioned that the working group would dedicate lines to each of the methodologies currently in use: molecular biology, RDTs, how to improve information and/or make it more accessible.

- Integrate environmental surveillance (e.g. using the qualitative microbial risk assessment framework) as part of cholera surveillance systems.
- Improve national surveillance capacity: develop and apply standards (case definition, measurements, e-formats, metadata, database design) and establish technical and institutional mechanisms for data exchange.

Oral cholera vaccines

Priorities for the first year of the GTFCC are shown below.

1. Generate information on use of OCVs in on-going immunization campaigns, particularly assessing the negative interactions between OCVs and other vaccines and ways to amalgamate OCVs with other vaccines/campaigns (e.g. piggybacking OCVs with other vaccines).
2. Determine how OCVs fit in the overall cholera control programme.
3. Ensure supply of OCVs for the global stockpile and beyond.
4. Promote policy to advocate for OCVs as part of an integrated strategy for cholera control (e.g. integration with the DOVE project).
5. Revise position paper to operationalize OCVs (and inform SAGE discussion).

Research agenda

- Determine the role of carriers in transmission of cholera and the impact of OCVs on carriers (mass immunization programmes).
- Determine the efficacy of OCVs in younger children, particularly those aged under 5 years.
- Develop an approach harmonized with the GAVI and SAGE guidelines to monitor and evaluate the impact of OCVs on the occurrence of cholera and operation of other cholera prevention strategies.
- The efficacy of OCVs stored at room temperature should be studied (or such an OCV should be developed), thereby bypassing the cold-chain requirement. The recent study in Guinea, published in the *New England Journal of Medicine*[5], showed that while the vaccine was refrigerated during storage, the cold chain was not maintained in the field, which did not appear to affect efficacy.
- Conduct research on improving the efficacy/lowering the costs of OCVs (long-term goal).

Case management

Priorities for the first year of the GTFCC are shown below.

[5] Luquero FJ, Grout L, Ciglenecki I, Sakoba K, Traore B, Heile M, et al. Use of *Vibrio cholerae* vaccine in an outbreak in Guinea. N Engl J Med. 2014;370:2111-2120. doi:10.1056/NEJMoa1312680.

1. Develop interim recommendations for treatment and gather evidence for the complete WHO guidelines on case management, including treatment.
   Output: Disseminate interim recommendations for case management.
2. Develop and implement a policy of in-depth investigation of all deaths, distinguishing the relative role of delayed help seeking, limited access to appropriate care and problems of case management.

   Output: Tool and guidelines for assessment in a social, behavioural and health system determinants of deaths.
3. Assess models of care in rural areas and those with dispersed populations by reviewing health services organization, community management and social messaging (collaborate with the fields of social mobilization and communication).
   Output: Conduct an assessment of existing evidence for models of care and develop methodology to gather the information.
4. Use of data to adjust interventions, collaborating with the fields of epidemiology and surveillance.

Research agenda

- Determine ideal ORS formulation for cholera patients (e.g. rice based vs routine ORS).
- Determine the role of antisecretory agents in cholera treatment.
- Describe and compare options for health services delivery in the context of different settings/conditions.

Further potential working group questions

Are there home remedies that the GTFCC can support?

Social mobilization

Priorities for the first year of the GTFCC are shown below.

1. Review existing materials, including those in other domains related to cholera (e.g. diarrhoeal diseases, Guinea worm): identify key messages; identify 'ideal' materials and pilot them in different regions, disseminating what works; identify country needs.
   Output: Publish key messages in a fact sheet; create a repository of (ideally field tested) messages and materials for use in emergencies and in endemic areas; publish a review of the links and synergies between social mobilization campaigns and long standing programmes such as diarrhoeal diseases.
2. Assess technologies, delivery systems (e.g. radio, SMS, theatre, women's groups) and other programmes (e.g. diarrhoeal diseases), and rate their effectiveness in reaching target audiences (e.g. were their messages internalized?).

   Output: publish a review of the literature and establish a research agenda

3. Define network surge capacity for emergencies and risk communication for long-term healthy behaviours; identify and disseminate the handbook on communication in emergencies; list in an accessible location the networks/stakeholders working in this field.

Conclusions

Most of the cholera control stakeholders invited to the meeting to revitalize the GTFCC were able to attend, indicating broad support for an updated task force, which can focus and catalyse support and action, and cholera control guidelines—taking action in the short- and medium-term to review and collect data and integrate strategies such as WASH with OCVs, supported by strong case management on a foundation of strong surveillance/epidemiology.

Lively discussion during day one of the meeting led to a number of important decisions being made about the structure and functioning of the GTFCC, particularly the membership of the GTFCC and the duties of its working groups. On day two participants presented updates and current challenges in six respective domains considered vital to cholera control: surveillance, epidemiology, OCVs, case management, WASH and communication/social mobilization. Staff from the Department of Epidemic and Pandemic Diseases then facilitated group work, dividing the participants into six areas based on those domains, to elucidate where future working group members could focus to achieve short-term gains (the so-called 'low-hanging fruit' which can be accomplished in 12 months), and lay out a research agenda for the future.

The presentations given on day two show that cholera control methods and risk factors, while complex and interdependent, are also known. The lack of access to clean water and adequate sanitation, for example, is a huge predictor of cholera transmission; those populations without adequate WASH are at high-risk for infection. However further research is needed to gather evidence on some strategies individually (e.g. spraying homes) or integration of strategies.

Many of those attending the first GTFCC meeting will be involved in the task force or its working groups going forward. It is envisioned that through broad stakeholder support, the revitalized GTFCC will keep cholera control on the public health agenda, disseminate current and emerging evidence on cholera control and coordinate integrated control efforts on behalf of WHO and other stakeholders.

Annex 1. Terms of reference of the GTFCC

Background

The 2011 WHA 64.15 resolution ("Cholera mechanisms for control and prevention") requested the WHO Director-General to revitalize the Global Task Force for Cholera Control ("GTFCC") and to strengthen WHO's work in this area, including improved collaboration and coordination among relevant WHO departments and other relevant stakeholders.

Status

The GTFCC is administered by the World Health Organization ("WHO") through its Department of Pandemic and Epidemic Diseases. The GTFCC is a collaborative mechanism between interested parties including WHO and GTFCC members, and is not an independent legal entity. For this reason, the GTFCC cannot conduct any actions in its own name. The operations of the GTFCC shall in all respects be administered in accordance with the WHO Constitution, WHO's Financial and Staff Regulations and Rules, Manual provisions, and applicable policies, procedures and practices.

1. Functions

Vision

GTFCC members share a vision that collective action can stop cholera transmission and end cholera deaths. The purpose of the GTFCC is to support increased implementation of evidence-based strategies to control cholera. The GTFCC aims to achieve this through strengthened international collaboration and improved coordination amongst stakeholders active in cholera-related activities.

GTFCC activities will aim to raise the visibility of cholera as a public health issue, facilitate sharing of evidence-based practices, and contribute to capacity development in all areas of cholera control. The GTFCC shall not be responsible for developing any technical norms or standards.

Objectives

The GTFCC members agree with the specific objectives of the GTFCC as stated below:

1. To support the design and implementation of global strategies to contribute to capacity development for cholera prevention and control globally.

2. To provide a forum for technical exchange, coordination, and cooperation on cholera-related activities to strengthen countries' capacity to prevent and control cholera, especially those related to implementation of proven effective strategies and monitoring of progress, dissemination and implementation of technical guidelines, operational manuals, etc.

3. To support the development of a research agenda with special emphasis on evaluating innovative approaches to cholera prevention and control in affected countries.

4. To increase the visibility of cholera as an important global public health problem through integration and dissemination of information about cholera prevention and control, and conducting advocacy and resource mobilization activities to support cholera prevention and control at national, regional, and global levels.

2. Membership

Members
At least for the initial phase, the GTFCC shall have 15 to 18 members, or less.

Members of the GTFCC will be identified and invited by WHO. The GTFCC will be open to institutions, including non-governmental and community-based organizations, international and intergovernmental organizations, universities, hospitals, and ministries. Members must demonstrate a clear interest and expertise on disciplines and perspective relating to cholera control. Relevant fields include, but are not limited to, epidemiology, public health, paediatrics, internal medicine, infectious diseases, water, sanitation, drug regulation, programme management, immunization delivery, health-care administration, logistics, communication, program evaluation and health economics.

Members may have a three-year membership in the GTFCC , which may be extended after the initial term. Any member may terminate its involvement in the GTFCC by providing written notice to WHO in its capacity as provider of Secretariat services to the GTFCC. In addition, WHO, in its discretion, may terminate the participation in the GTFCC of any member.

The GTFCC will select from amongst its members a Chairperson. The Chairperson of GTFCC is expected to serve as Chairperson for three years. After the initial selection of a Chairperson, future Chairs will need to have served as a member of GTFCC for a minimum of one year before taking up Chairmanship.

GTFCC participation is open and on a voluntary basis. No dues will be charged. All member organizations agree to promote the provisions of WHA 64.15 and abide by these Terms of Reference.

3. Management

Secretariat support
Secretariat and planning support of the GTFCC will be provided by WHO acting through the Department of Pandemic and Epidemic Diseases (hereinafter referred to as the "Secretariat").

Information exchange
The GTFCC will normally meet biannually and may utilize face-to-face, teleconferences or other electronic communication meeting methods. Special meetings may be called to address emerging issues. Meetings and Teleconferences will be convened by the Secretariat and can be hosted by members as agreed.

Decision-making
Decisions concerning GTFCC activities will, as a rule, be taken by consensus. WHO shall fully participate in the decision-making process and shall have the right to veto any decision that is contrary to its policies, rules, regulations and administrative procedures.

Working groups and experts
GTFCC Working Groups may be established as resources intended to increase the effectiveness of GTFCC. The Working groups are established to prioritize issues within a particular area and to mobilize external expertise for answering specific questions identified by GTFCC when the issue is particularly complicated and additional time, expertise, and discussion are required. Iindividual experts may be consulted and/or invited by the Secretariat to provide advice to WHO on specific technical issues in accordance with WHO rules and procedures.

Financing of and fundraising for the GTFCC
GTFCC members will not be remunerated for their participation in GTFCC. Each member is, in principle, responsible for meeting its own expenses in relation to the GTFCC (including, but not limited to, travel and subsistence for the attendance of GTFCC meetings).

All activities undertaken by the GTFCC, as opposed to those undertaken by GTFCC members in their individual capacities, including its day-to-day operations and the Secretariat support, are subject to the GTFCC Secretariat receiving adequate funds for that purpose.

Finally, WHO may also raise funds from other sources to support the work of the GTFCC, in accordance with WHO's established policies and principles.

All GTFCC Secretariat funds shall be administered in accordance with WHO's financial regulations, rules, and practices and is subject to WHO's normal programme support costs.

4. Information and documentation

Publication
As a general rule and subject to its discretion, WHO shall be responsible for issuing publications about GTFCC activities. All decisions about the preparation and dissemination of publications made by GTFCC Members (other than WHO) concerning GTFCC activities shall be made by consensus.

Copyright in any publication made by WHO shall be vested in WHO. This also applies if the work is issued by WHO and is a compilation of works by GTFCC Members or is otherwise work prepared with input from one or more GTFCC Members. Copyright in a specific separable work prepared by a GTFCC Member shall remain vested in that Member (or remain in the public domain, if applicable), even if it forms part of another work that is published by WHO and of which WHO owns the copyright as a whole.

Copyright in a publication prepared and issued by a GTFCC member shall remain vested in that member or shall be put in the public domain if such GTFCC member so chooses.

"Publications" include any form, whether paper or electronic, and in any manner. Parties are always allowed to cite or refer to GTFCC publications, except for purpose of promoting any commercial products, services or entities.

Any publication about GTFCC activities issued by a GTFCC Member other than WHO shall contain appropriate disclaimers as decided by WHO, including that the content does not necessarily reflect the views or stated policy of the participating organizations, agencies and institutions (including WHO, acting as the Secretariat for the GTFCC).

Communication
The conclusions of GTFCC meetings shall be made public, including through the Weekly Epidemiological Record and WHO web site.

GTFCC Members shall not make public statements about GTFCC activities or public statements on behalf of WHO unless specifically requested to do so by WHO.

The contributions to the GTFCC made by GTFCC Members will be acknowledged by WHO in accordance with it applicable rules, policies and practices.

Confidentiality:
GTFCC Members agree:

- To maintain confidentiality of information shared among GTFCC Members, except when explicitly indicated otherwise by WHO;

- To maintain confidentiality about views of the various Members and the deliberations of the GTFCC, except with regard to agreed statements and reports issued by WHO or with the consent of WHO; and

- Not to make public statements about GTFCC activities or public statements on behalf of WHO unless specifically requested to do so by WHO or with the prior consent of WHO.

Liability
Under no circumstances shall WHO assume any liability for acts carried out by GTFCC Members regardless of whether such acts were carried out

in the name of the GTFCC. Furthermore, WHO in its sole discretion, may refrain from implementing any decision of the GTFCC if in the view of WHO, such decision gives rise to undue financial, legal or reputational liability or is contrary to WHO Rules, Regulations Administrative practices and programmatic and technical policies.

Amendments

These Terms of Reference may be amended by WHO and all GTFCC Members shall be informed of such changes and shall be required to endorse them as a condition for their continuous participation in the GTFCC.

Annex 2. Meeting programme and list of partners

Meeting programme

Day 1		
8.30 – 9.00	Welcome Coffee	
9.00 – 9.15	Opening	Sylvie Briand, Director PED
9.15 – 9.30	Appointment of a chairperson for the meeting Introduction of participants	Chairperson
Introduction of the GTFCC		
9.30 – 10.00	History of the GTFCC: development, working group, stakeholder analysis	Alan Hinman
10.00 – 10.30	Status of the GTFCC and TORs	Anais Legand, PED
10.30 – 11.00	Coffee break	
11.00 – 11.30	GTFCC objectives	William Perea, Coordinator CED/PED
11.30 – 13.00	Management of the GTFCC: membership and chair, functioning and secretariat, working groups, meetings, communication, decision making, resources	Chairperson
13.00 – 14.00	Lunch break	
14.00 – 15.00	Management of the GTFCC (cont.)	Chairperson
15.00 – 15.30	Coffee break	
15.30 – 17.00	Management of the GTFCC (cont.)	Chairperson

Day 2		
Methods for cholera control: situation analysis and priorities for action		
9.00 – 9.30	Situation of cholera in WHO regions	WHO ROs
9.30 – 10.00	Epidemiology of cholera	Eric Mintz, CDC
10.00 – 10.30	WASH	Daniele Lantagne, Tufts University
10.30 – 11.00	Coffee break	

11.00 – 11.30	Surveillance	Martin Mengel, AMP
11.30 – 12.00	Oral Cholera Vaccines	Balakrish Nair, Translational Health Science and Technology Institute
12.00 – 12.30	Case management	Myriam Henkens, MSF
12.30 – 13.00	Social Mobilization	Amanda McClelland, IFRC Kate Alberti, UNICEF
13.00 – 14.00	Lunch break	
The way forward		
14.00 – 14.15	Introduction of group work	Dominique Legros, CED/PED
14.15 – 15.30	GTFCC working groups, priorities and timeframe	Group work
15.30 – 16.30	Feedback from the groups and conclusions	Chairperson
16.30	Closure	

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