GLOBAL TASK FORCE ON
CHOLERA CONTROL

REPORT OF THE

9TH MEETING OF THE GLOBAL TASK FORCE ON CHOLERA CONTROL WORKING GROUP ON ORAL CHOLERA VACCINE

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Acronyms and abbreviations

AEFI	adverse events following immunization
AMR	antimicrobial resistance
AWD	acute watery diarrhoea
CATI	case-area targeted intervention
CCV	cholera conjugate vaccine
CE	community engagement
CFR	case fatality rate
CMO	contract manufacturing organization
CSP	GTFCC Country Support Platform
CTC	controlled temperature chain
DRC	Democratic Republic of Congo
EPI	WHO Expanded Programme on Immunization
GAVI	Global Alliance for Vaccines and Immunization
GMP	good manufacturing practice
GTFCC	Global Task Force on Cholera Control
icddr'b	International Centre for Diarrhoeal Disease Research, Bangladesh
ICG	International Coordinating Group
IDP	internally displaced people
IFRC	International Federation of Red Cross and Red Crescent societies
IPC	infection prevention and control
IRP	Independent Review Panel
IVI	International Vaccine Institute
JHU	Johns Hopkins University
KAP	knowledge, attitudes and practices
LSHTM	London School of Hygiene and Tropical Medicine
M&E	monitoring and evaluation
MSF	Médécins Sans Frontières
NCP	national cholera plan
OCV	oral cholera vaccine
ORT	oral rehydration therapy
PQ	WHO pre-qualification
R&D	research and development
RCCE	risk communication and community engagement
RCT	randomized control trial
RDT	rapid diagnostic test
RRT	rapid response team
SAGE	WHO Strategic Advisory Group of Experts on Immunization
SDGs	Sustainable Development Goals
SIA	supplementary immunization activities
SOPs	standard operating procedures
US CDC	US Centers for Disease Control and Prevention
US NIH	US National Institutes of Health
VIS	Gavi Vaccines Investment Strategy
EWARS	early warning alert and surveillance
WASH	water, sanitation and hygiene

Executive summary

The ninth annual meeting of the Global Task Force on Cholera Control (GTFCC) working group on oral cholera vaccine (OCV) took place at Les Pensières, Annecy during 11-12 October 2022. The meeting was conducted as a hybrid of in-person and virtual attendance. Attendees included working group members from technical partners, donor organizations, UN agencies, non-governmental organizations (NGOs) and countries affected by cholera. The objectives of the meeting were to:

- provide an update on the global cholera and OCV situation;
- review the main obstacles experienced during 2022;
- celebrate partner and country successes;
- receive 5-year OCV forecasts from countries;
- review progress on research priorities;
- review progress on the OCV working group guidance currently in development;
- discuss guiding principles for OCV allocation; and
- ratify WG priorities for 2023.

Through mid-2021 there was an unexpected cholera resurgence, with lab-confirmed outbreaks in 23 countries, including some that had seen no cases for years, and some nations and regions experiencing their largest outbreaks in decades. This triggered extensive support to countries from WHO and the GTFCC partnership that exhausted national and international response capacities, demand for OCV and other cholera commodities exceeding available supply . Preliminary data for 2022 suggests a similar situation, if not a worse one. At the time of the meeting, 28 countries, including 12 countries that had not reported a cholera outbreak in 2021 had reported having a cholera outbreak in 2022. Of the 23 countries that experienced a cholera outbreak in 2021, 19 (83%) reported another cholera outbreak in 2022. The largest outbreaks seen in years took place in parts of Africa, the Indian subcontinent and the middle east, with many countries (including Haiti, Syria and Lebanon) affected after many years being cholera-free. The surge in cholera outbreaks threatens progress towards cholera control as resources, including OCV, are focused on outbreak response rather than preventive efforts. In light of this situation, the meeting heard from the International Coordinating Group (ICG) about the decision to move temporarily to a one-dose outbreak response strategy, a decision later announced publicly by WHO[1].

The meeting heard how the process for requesting doses for preventive OCV campaigns will move from GTFCC to Gavi; how the new process will work; and how the transition period is expected to be managed. Discussion sessions examined countries' lessons and experiences in integrating other cholera control interventions with OCV, the guiding principles for allocating OCV during emergencies, and development of multiyear vaccination plans.

Elsewhere in the meeting a range of issues emerged (or re-emerged) as prominent themes in the discussions that should shape the GTFCC's work in the coming months and years. These included future vaccine demand projections and the importance of this for increasing vaccine supply; the need to update the ICG's guidance, forms, and processes for requesting OCV for emergency response, and to communicate better to countries; the need to develop a framework for OCV allocation; and the need for better communications from the cholera research community to the GTFCC – perhaps showing that improved communication between different stakeholders in the cholera community would be welcome all round.

[1] https://www.who.int/fr/news/item/19-10-2022-shortage-of-cholera-vaccines-leads-to-temporary-suspension-of-two-dose-strategy--as-cases-rise-worldwide

The meeting closed with a round of thanks to participants, donors and partners for their continued support of work to achieve the goals of the GTFCC core document, *Ending cholera: a global roadmap to 2030.*

Welcome & introductions

The meeting opened with an introduction from Lucy Breakwell (US Centers for Disease Control and Prevention/US CDC), chair of the working group, who emphasized the importance of increasing focus on countries' activities and needs. Participants then all introduced themselves, breaking the ice with – among other things – a short description of what drink they take in the mornings.

There are a lot of coffee drinkers in the OCV working group.

Overview of OCV use in 2022

***Malika Bouhénia**, WHO OCV focal point; **Philippe Barboza**, WHO Cholera Team Lead*

Dr Barboza opened with a simple reminder of how unacceptable the current situation has become: rising infections, illness and avoidable cholera deaths.

Mid-2021 saw an unexpected cholera resurgence. Twenty-three countries experienced lab-confirmed outbreaks, including some that had seen no cases for years. West Africa experienced its largest outbreaks in decades, particularly in Nigeria and Niger. In 2021, 30 countries reported autochthonous cases, with only five imported cases in total (though some, like India, did not report). The big picture was one of an overall increase in cases, deaths, and case fatality rate (CFR), which is overall likely a gross underrepresentation of the true cholera burden, especially in Asia. As well as known intrinsic risk factors, this situation was triggered and sustained by a wide range of external factors including but not limited to conflict, humanitarian crises, climate change and natural disasters, and the many and varied impacts of the COVID-19 pandemic on public health and access to services. Throughout 2021 the cholera resurgence triggered massive support to countries from WHO, the GTFCC and its partners, exhausting national and international response capacities, resulting in shortages of cholera commodities, and prioritization of the available OCV supply for outbreak response.

Preliminary data for 2022 suggests a similar situation. To date 28 countries, including 12 new ones, had reported outbreaks since the beginning of 2022. Only four countries with outbreaks in 2021 did not report another cholera outbreak in 2022. The largest outbreaks seen in years took place in parts of Africa, the Indian subcontinent and the middle east, with many countries (including Haiti, Syria and Lebanon) affected after many years being cholera-free.

In 2022, 33 million doses had been requested from the OCV vaccine stockpile by the time of the meeting, of which 24m had been approved. These included one preventive request for 10m doses for Nigeria, which was received in December 2021 and approved in 2022, and 12 emergency requests from Cameroon (two requests), Malawi, Bangladesh, Somalia, Pakistan (four), Kenya (2), and South Sudan. Ten emergency requests totalling 14m doses were approved, two requests from Kenya and South Sudan in response to emergency humanitarian contexts versus outbreak response were not approved. So far, 23.5m doses have been shipped in 2022, of which 20m were for emergency use to 12 countries. In 2022, two preventive campaigns were implemented, one in South Sudan and one in Nigeria. For emergency campaigns, 2 dose campaigns were implemented in Nepal, Cameroon, Bangladesh and Somalia, first dose campaigns were completed in Pakistan, Malawi and Cameroon, and second dose campaigns from 2021 requests were implemented in Nigeria, Ethiopia and Yemen. Common challenges with campaign implementation included delays between receipt of doses and campaign implementation, low two-dose coverage, and lack of post-campaign coverage surveys.

The observed cholera resurgence is further straining the already constrained supply of OCV doses. More OCV doses have been approved, for both preventive and reactive campaigns, than are available (35m in total). Current stock at the time of the meeting was 5.3m doses (with the emergency stockpile meant to remain at 5m doses), with a further 6.8m doses expected to be produced between October and December. At the time of the meeting, 8m doses were still needed to complete approved emergency second dose campaigns. This did not account for any doses that may be needed for recently reported outbreaks. In light of this situation, discussions at ICG level resulted in the decision to move temporarily to a one-dose strategy to be able to respond to current and anticipated outbreaks (this decision was announced to the working group at the end of the meeting).

Country engagement to achieve the goals of the GTFCC core document, *Ending cholera: a global roadmap to 2030* (aka "the roadmap") has been increasing, despite the pressures of COVID-19. To date, 15 countries (seven of which completed the exercise in 2021/2022) have completed their cholera hotspot mapping, with a further six in process at the time of the meeting. Seventeen countries have completed their national cholera control plans (NCPs), with a further 12 countries in process and six more considering NCP development.

GTFCC partners are engaged and active in the cholera response in all settings, though more is always needed. As just one example of such action, over 30% of all cholera cases in Nigeria in 2021 were treated by Médécins sans Frontières (MSF). Partners' work is limited, as always, by the scarcity of resources, structural challenges (such as poor WASH coverage and inadequate surveillance) and other issues, including insecurity.

Discussion

- There was a general concern about the proportion of OCV doses being used for emergency campaigns and consequently the lack of progress with implementing preventive campaigns. Particularly in relation to the impact this has on manufacturers perceived risk of the cholera vaccine market. It was suggested to communicate, especially to manufacturers, that the lack of prevention requests in 2022 has been mainly due to the need to respond to emergencies, not poor planning, and to countries deciding not to make requests because they know that OCV stock is low. The latter being seen more frequently: demand is adapting to supply.
- It was discussed that the working group will need to better document potential demand to better inform and reassure manufacturers. There was a suggestion for countries to request the number of doses they need, even if they know that the current supply could not support the request. However, this needs to be balanced with the burden of work associated with completing and reviewing these requests. Another suggestion was for Gavi to explore opportunities to document intent of countries, as has been done for other vaccines to obtain a high-level picture of demand.
- The ways in which the working group could support the demand side was also discussed. To help stabilize and better anticipate the global OCV demand, the working group has been supporting several countries (DRC, Cameroon, Kenya) to identify their cholera hotspots and develop multiyear vaccination plans (MYPs). 3 countries are expected to submit their vaccine requests to Gavi during 2022 (Cameroon, DRC, Mozambique. The working group should continue to support countries to complete their hotspot analysis and prepare NCPs to ultimately move forward on the pathway to be able to request vaccine for preventive campaigns. The OCV strategy (under development) will help GTFCC partners focus efforts to support countries that have prioritized preventive OCV use submit high quality requests in the next year or two.
- Despite the focus on OCV, partners discussed the importance of appropriate treatment and that efforts to reduce mortality should not be overlooked and must be supported. The GTFCC relies on its partners' ability to implement or support case management – a task challenged by many things, including conflict, crisis, and accessibility issues, that are under no-one's control. The GTFCC and

WHO are communicating with the wider UN ecosystem about the division of responsibility. This is further complicated by temporal shortages in cholera response commodities.

- Other major topics of discussion included:
    - Climate change is no longer a risk but a reality, with large weather events linked to increased cholera. Malawi is one example, where good progress in outbreak control was almost completely reset by two successive cyclones that destroyed key infrastructure. Though a huge factor, climate change is poorly understood and its effects difficult to predict.
    - Cholera prevention and response lie on a continuum: emergency and prevention should not be opposed. However, given the highly constrained supply, it will be critical to review and make evidence informed decisions to determine the most impactful use of the limited OCV supply.

Country perspectives on OCV use in 2022

In this session country representatives discussed their experiences of planning and implementing campaigns, vaccine allocation, their successes and lessons, and the challenges they have encountered.

Ethiopia

Challenges

Ethiopia has experienced issues around campaign implementation timeliness due to problems associated with the Ethiopian system as well as issues in the pre-importation phase, after vaccine doses reach the airport.

The large number of national actors working on implementation, transport and other campaign activities often makes planning and execution of campaigns more challenging. The ministry of health (MOH) is working to decrease the number and range of actors playing different campaign roles, which may help keep to time.

Emergency campaigns are not planned but implemented as soon as vaccines are received. This can happen in a context with dozens of parallel interventions going on at the same time – other immunization campaigns, deworming drives, etc. – which can present serious problems, such as a lack of vaccine storage space at woreda (local administrative) level.

Security and conflict are also currently problems in Ethiopia.

Delay in receipt of second doses, is a major issue, as is the late release of operational funds, often 2-3 months after implementation of the campaign, which can reduce the quality of the campaign.

Impact

An impact study of OCV campaign is in preparation. Ethiopia has received a good amount of doses over the last three years: pending the results of the assessment, the country has not seen further outbreaks in most campaign areas. Only two outbreaks have so far been seen in woredas that previously had campaigns, with none in the other 52+ vaccinated woredas. Among other things, the assessment will aim to identify what went wrong in the two exceptions.

Nepal

Challenges

Internal issues in Nepal have been similar to those seen in Ethiopia. Outbreaks occur almost annually, and the country has experience of vaccinating in different districts. A 2021 outbreak along the Indian border resulted in an application for reactive doses but hit familiar challenges: the campaign was at the peak of the COVID-19 vaccine drive, diverting staff and resources and stressing cold chain capacity. This was managed with ingenuity and alternative resources. In the first phase of the campaign, where people saw cholera cases and complications around them, there was huge participation, with coverage of over 90%. In the second phase, however, acceptance was poor and coverage fell to around 70%.

It is challenging to mobilise enough resources for the necessary campaigns. Nepal, like other countries, has many other priorities and ongoing, parallel public health campaigns, which always makes planning and execution difficult.

Lessons

In one district, Nepal had interesting results experimenting with self-administration of second doses. Patients were given their second dose along with the first, instructed in how to store it at home, and told when to administer it. The results – while not yet published – were highly encouraging, and the administration rate for second doses in this campaign was around 80%. This is useful learning for reactive planning.

Bangladesh

Challenges

Cold chain has been a constant challenge in Bangladesh, mainly because of competition from COVID vaccination campaigns.

Lessons

Outbreaks happen almost every year in different parts of country. To meet this recurring need, Bangladesh needs an effective supply chain that can reliably provide first and second doses to the point of care at the same time, thereby reducing costs.

Bangladesh has bimodal peaks, which are difficult to handle, and some areas are suffering very badly from the effects of climate change.

Bangladesh is continuing to work on its NCP, and with help of partners has already redefined the NCP priorities once.

Volunteers and UN and other development partners have helped hugely with the planning and administration of campaigns. Bangladesh is fortunate to have a very good multidisciplinary team supporting cholera control. With continued support from the ICG and the GTFCC, Bangladesh believes it can contain cholera.

Democratic Republic of Congo (DRC)

Challenges and lessons

In 2018, DRC vaccinated certain districts that have since seen outbreaks despite these campaigns. Vaccination must be reinforced in these areas. To do this, DRC is developing a post-NCP three-year plan to reinforce preventive vaccination. If the country continues to focus only on reactive campaigns, little

progress will be made: experience suggests that doses only arrive once outbreaks are already out of control.

Water, sanitation and hygiene (WASH) implementation also needs to be improved, with clear orientation for WASH programmes. At the moment, different districts are choosing different WASH strategies, with little coordination.

The most pressing overarching question in DRC is whether or not it would be more effective, and feasible, to health zone coverage to prioritize the needs of target health districts.

South Sudan

Thanks to positive GTFCC responses to most preventive requests, South Sudan has carried out OCV campaigns in five locations across 20 hotspots to date. This work continues. In the most recent outbreak, prior GTFCC approval for preventive vaccination meant doses were already in place, and the campaigns were done well. An outbreak occurred in that location, but cases were low and there was only one death. Experience shows that the perceived impact of these campaigns is immense.

Challenges and lessons

The target population has been overestimated in most locations so far, leading to large numbers of leftover doses at the end of the campaign. So far, when this has happened, South Sudan has requested that the GTFCC to allow these to be used in other hotspots, permission has been granted, and the doses have been used.

Continued flooding in most locations affects implementation, causing logistical and access challenges and increased risk of transmission. This underlines the importance of receiving vaccines for emergency response as quickly as possible after a request – in the wet season many places cannot be accessed at all because of flooding.

Cold chain challenges are similar to experiences described elsewhere. Because of ongoing COVID vaccination, South Sudan has inadequate capacity to store OCV. The solution has been to receive doses in phases so as not to overload the cold chain.

In-country shipment remains challenging, mainly due to funding challenges affecting partners supporting transport. South Sudan is currently looking at ways to include funding for domestic shipping in vaccine requests.

At the end of every campaign, an independent post campaign evaluation is done to assess coverage.

Mozambique

Challenges and lessons

The main lesson of the Mozambique experience is that difficulties tend to occur *after* vaccines reach the country.

Mozambique's main problem has been a lack of domestic registration for the vaccine, leading to delayed implementation in emergency situations because of issues obtaining import waivers.

Operational resources – not just cash – are scarce. The scope of this issue was laid bare during recent cyclones, when – due to the emergency – WHO, MSF and others were in place with resources that are usually lacking: the means to transport vaccine, technicians to administer them, and support for

communities to help implementation. This underlined how much Mozambique is normally constrained by a lack of resources and capacity.

Coordination is also difficult. Implementation of campaigns tends to start well, but once vaccines are moving out to the districts, it gets harder. Campaigns are affected by competing priorities for the MOH and its partners, and restrictions on vehicle use and supplies cause delays. Experience shows that planning and coordination take on a different light once implementation starts - the reality of hitting the ground can make a considerable difference. Poor coordination means poor reporting: different teams produce reports and it is impossible for the ministry to track which are submitted. It has frequently been necessary to contact the GTFCC secretariat directly to sort out the ensuing confusion.

Outbreaks in north Mozambique present further challenges, some taking place in areas completely inaccessible by vehicle. This makes planning and allocation different from normal campaigns, and the national team does not currently know how to address it.

ICG perspective: OCV challenges and workplan

***Salim Mohammad Reza**, ICG secretariat*

The core mandate of the ICG is to ensure availability of, and equitable access to, licensed vaccines for cholera, meningitis, yellow fever, and Ebola virus disease during outbreaks. The ICG mechanism tries to ensure quick, targeted deployment so vaccines can be used where they are most needed.

Since 2016 the OCV emergency stockpile has shipped over 55m doses to 20 countries. The two-day target for the ICG decision making process on emergency requests has been met in 89% of requests in that time, and in 97% of requests since 2018. The main challenge throughout this period has been high demand versus low supply. Several possible solutions have been considered, including increasing the size of the stockpile; only shipping first-round doses; making supply of second doses conditional on submission of a first-round campaign report, real time availability and/or potential demand (as measured by ongoing outbreaks and ICG requests in the pipeline); and partial approval of some requests.

In the ICG annual meeting in September 2018, members decided to increase the OCV emergency stockpile size from 2m to 3m doses, to be available at all times, effective from 2019. In the annual meeting in September 2021, the members increased the stockpile further, from 3m to 5m million doses, effective from 2022. Challenges to stockpile management have included delayed arrival of vaccines in countries (mainly due to unavailability of cargo flights, lack of cold chain capacity at destination, and import clearances) and late implementation of campaigns – mainly due to operational issues, funding, loss of priority to other diseases, and the inaccessibility and/or security context of the target populations.

The ICG workplan for OCV for 2022-2023 is as follows:

- Making the ICG OCV request form and annexes simpler and more user-friendly
- Providing OpenWHO trainings on the ICG mechanism and a guideline for filling the ICG request form
- Building the capacity of stakeholders, mainly through on-site training courses in high priority countries
- Organizing three-level technical calls and meetings between ICG members and country teams when appropriate
- Improving partner engagement and coordinating with ICG member organizations to provide field support for vaccination campaigns.

More information on the ICG can be found at the following links:

https://www.who.int/groups/icg/cholera

https://openwho.org/courses/introduction-icg-and-mechanism

Discussion

- **The size of requests has increased over time.** It is impossible to say why, as data is lacking, but that understanding this increase would be valuable. There are several hypotheses, including that outbreaks are getting larger and more explosive; that requests are arriving late, further along the epi curve than they should be; and that countries were making insufficient requests before, or are over-requesting now. The size of the country is also an element – recent outbreaks have taken place in very large countries such as Bangladesh, Ethiopia and Nigeria. These and other explanations could be concurrent, but the solutions to each may be different. More analysis is needed, but the likelihood is that several different factors are at play. More countries engaging in cholera control, and delays in detection and identification are a recurrent problem. Stronger surveillance is critical to addressing these issues.
- Delayed request submission. One reason for this is the challenge of finding the right areas to vaccinate, including defining a sufficient buffer zone around the outbreak to prevent the future need for more vaccination.
- Delayed implementation.
- 2020 was an important year as well, not so much for the lack of availability of doses but because the volatility of programmes meant high volumes of vaccines remained sitting with suppliers.

Guiding principles for OCV allocation in emergencies

2022 has seen several requests for OCV that were not approved. This session discussed whether it is in fact necessary to vaccinate in response to all outbreaks.

Discussion

- **OCV** is a tool for outbreak response and **is most effective if used as soon as possible** after a cholera outbreak has been identified. If applied late in the outbreak, it is not as effective. It is not the only tool, however, and while it should be considered as part of a package of emergency response to help control an outbreak, it cannot replace WASH, surveillance, early case identification and good case management. If the question was "should *only* OCV be used", the answer is "no"; but if the question is whether it should be offered as part of a balanced package, then "yes". The group discussed and agreed that there are situations where it is not appropriate, but that OCV use should be considered in every outbreak. If OCV is not considered at the start of the outbreak response, the opportunity for the vaccine to have an impact is missed. Considerations around when to use OCV will depend on context: some countries need vaccination after a single case; in others it may make sense to wait for a confirmed outbreak before vaccinating.
- Partners raised the **need to provide better guidance for countries** on when and where to vaccinate. Countries always have questions about how to prioritize areas for reactive vaccination. OCV is best considered in complex situations, with high movement of populations, where other interventions alone cannot reduce cases. Experience shows that it should be used alongside complementary strategies. However, when cases and deaths are mounting, countries may

request OCV regardless of if it is the most appropriate use of OCV. Further discussion between the working group and the ICG secretariat on this was seen as a priority for 2023.

- There were concerns that advocating for countries to consider OCV for every single outbreak could unintentionally reduce the perceived importance of other interventions, especially WASH. Experience does suggest that OCV use and reduction of cases in vaccinated areas can lead to the assumption that other interventions are not needed. This is a strong argument not to recommend controlling every outbreak with OCV, especially where population movement is predictable and controlled, and simple providing safe water can drastically reduce cases without vaccination.
- **Delays in request submission**. There is often a long delay between identifying an outbreak and submitting a request. Situations evolve and countries must assess them, but it is important to draw a line and submit requests in time. A known lack of information is useful information in itself, and countries should feel able to say when they do not have it.
    - **Case confirmation** is important in this process, and in many contexts confirming cholera takes far too long. New and better confirmation methods are therefore needed. A simple thing that would make a huge difference in places with poor or slow lab access would be a guideline on how many positive RDTs it takes to provide confidence of cholera without waiting for a laboratory confirmation.
    - **Diagnosis is a challenge**. Prevention and elimination plans must improve surveillance and diagnostic capacity, moving beyond the uncertainty of acute watery diarrhoea (AWD). If cholera can be identified more quickly, decisions can be made more quickly, and coordination mechanisms and implementation can be fast tracked. If that process is too slow – and this happens in many contexts, whether because of COVID-19 or other overlapping outbreaks – the criteria can change several times, meaning that by the time requests are received the epidemic has changed and the opportunity to control it has been lost.
- Many countries seem unaware that there is a mechanism that provides **flexibility to modify ICG requests** (probably because this is not explicit in the guidelines). If an outbreak changes during the application process, countries can notify the ICG in writing within one day. They should feel free to adapt to changing situations, and the flexibility is there for exactly that purpose. It is, however, important not to use ICG vaccines on a project other than the one that was approved without informing the ICG first.
- While countries have been told by the GTFCC to submit quickly even when there are information gaps – in effect told not to "write a thesis" – it can often seem like an application without such a thesis will not get doses. Explicit **guidance is needed on the minimum information thresholds** that guarantee high consideration to receive doses if they are available. At present, seemingly without regard to the quality of the application or the level of effort that went into it, countries are not made aware of why their applications fail.
- The planned online training on how to populate the ICG request will be very helpful. Some of these issues are already addressed in examples given in existing ICG training (e.g., case studies of insufficient information versus too much information that delays the request). Countries often struggle to find the right level, and the ICG secretariat is working on making request submission processes easier. Delays are often not so much a question of the nature of the application as one of the time invested in it, which is often enormous.
- Something important that **requests often lack is the unique contextual insight** that countries should be able to provide about their own situation, leaving the ICG to fill the gaps. This hugely valuable information is far better from the source, but it is rare that applications talk about the people affected, their social issues and their contexts (e.g., specific movements and social groupings, local dynamics, predicted movements, etc.).
- There is also a need for systems by which country situations can be monitored, to keep abreast of additional support needs. Most contexts are extremely difficult, and it is important to share challenges, strategies used and those which worked, and any other questions that need to be answered.

- Countries should be clear with the GTFCC and with partners about where they need help to be able to make more timely decisions – outlining the nature of the challenges in different countries, the difficulties in identifying the right points, and where and how best to request and implement OCV. The earlier a request is submitted, the smaller the outbreak, and the smaller the request can be.

ICG Guidelines on use of OCV stockpile for emergency response

***Lucy Breakwell**, US CDC and OCV Working Group Chair*

Breakwell gave a short presentation summarizing the available ICG guidelines for emergency OCV requests. The guidelines were developed in 2013, and do not reflect current practices for prioritizing areas for OCV use in emergency, particularly outbreak, situations. In brief, the 2013 guidelines recommend targeted vaccination to supplement the mainstays of cholera outbreak control (case management, WASH and community mobilization) and to limit the spread of outbreaks in communities at imminent risk, such as communities in neighbouring areas across borders and/or linked by river or WASH systems. This is because vaccination was thought to have greater impact in these areas then in areas with active transmission (weeks or months) where many individuals may have already been infected, including asymptomatic infections (80% of cholera infections are asymptomatic). The guidelines also recommend considering reactive vaccination for areas where response mechanisms cannot deliver typical cholera control measures.

Figure 1: OCV decision making for health authorities described in 2013 ICG guidelines

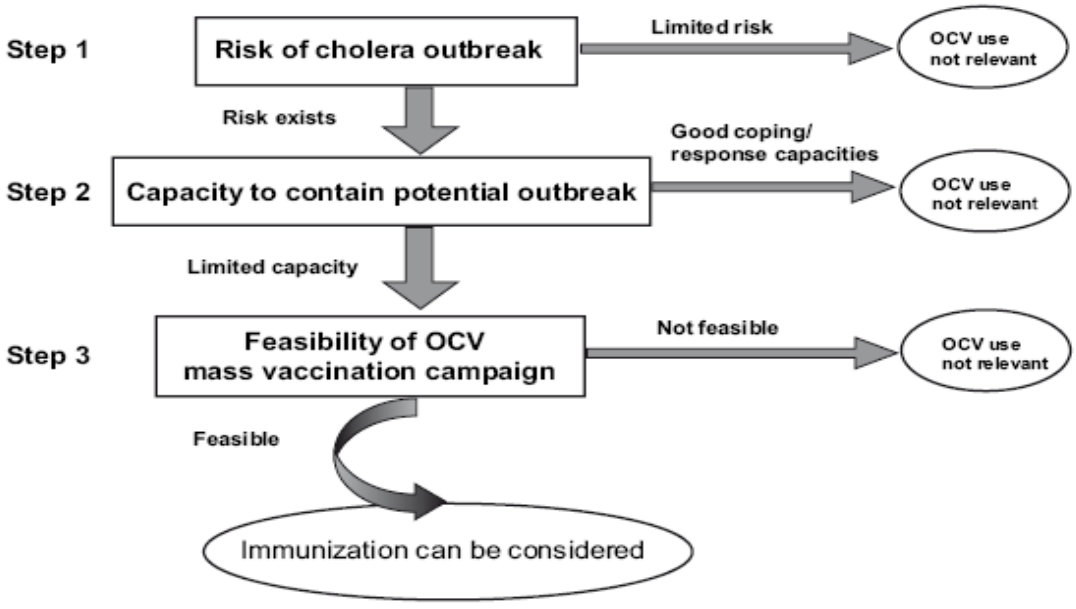


Figure 2: ICG decision criteria for the release of OCV, 2013 ICG guidelines

Criterion	Indicator	Potential impact of OCV campaign	
		High	Low
Susceptibility of the population	• Number of cases reported in the affected area(s) during the past 2–3 years • Attack rate of previous outbreaks in the affected area(s)	No or few cases	High number of cases
		High attack rate	Low attack rate
Vulnerability of the population	• Case-fatality rate (CFR) of previous outbreaks in the affected area(s) • Refugee camp, internally displaced people, or slums present in the affected area(s) • Area(s) with important population movements (border, market hub, etc.) • Population density in the affected area(s) • Access to water, sanitation, and hygiene	High CFR	Low CFR
		Yes	No
		Yes	No
		High density	Low density
		Poor access	Good access
Risk of spatial extension	• Time elapsed / maturity of the outbreak since first case reported • Attack rate since the start of the current outbreak (i.e. cumulative cases) • Proportion of health units in the district reporting cases • Time at which first cases were notified during the epidemic season	Few weeks	Few months
		Low attack rate	High attack rate
		Low proportion	High proportion
		First cases notified early	First cases notified late

Discussion

- An update of the guidelines is overdue. This year, OCV campaigns have prioritized children and mobile populations, but these prioritization categories can change and it is difficult to balance them across all countries. These guidelines were developed without any data on implementation and use. When the stockpile was created there were no preventive OCV programmes, and therefore no attempt to address them. Now, however, there is an opportunity to use a decade's worth of data and experience to inform revisions to the guidelines.
- It is important to examine and clarify the underlying rationale for handling requests so that all stakeholders have a clear understanding. This is a key need, because without it everyone is wasting energy trying to connect the dots. That explanation can be brief, but it must be present and explicit.
- To end the session, participants were invited to participate in an online poll gathering short sentences specifying the contexts in which they felt it was most important to prioritize OCV. The contexts that emerged included areas of high population movement; areas with high risk of spread (raising questions about how to define that risk); areas without WASH; and humanitarian contexts.

Poster preview

This session consisted of a short preview of the poster exhibition that was in place throughout the meeting.

Progress on OCV Working Group activities in 2022

***Lucy Breakwell**, US CDC and OCV Working Group Chair*

Dr Breakwell gave a brief presentation of the 2022 workplan, divided across four thematic areas as follows:

- Guidance
    - Selection of identified hotspots for OCV use (part of MYPs)
    - Strengthening the GTFCC process for reviewing preventive OCV requests
- Operations
    - Preparing training materials and conducting training on OCV for ministries and consultants
    - Developing tools and guidance documents to ensure standardized M&E of campaigns
    - Conditionality on supply for Euvichol-Plus: obtaining data/information by June 2022
    - Developing a transparent and fair process to prioritize OCV shipments due during supply constraints
- Data sharing
    - Developing a dashboard for OCV requests, shipments, and campaigns
    - Reviewing OCV use 2013-2021
    - Reviewing impact of COVID-19 on OCV campaigns
- Research
    - *A full report of the research activity is provided in the next section of this document.*

Selecting hotspots for OCV MYPs

A sub-working group was set up in 2022 to develop criteria to select and prioritize cholera hotspots identified through the GTFCC hotspot tool for OCV preventative campaigns to inform national multi-year vaccination plans. The sub-working group held a series of meetings between January and April 2022 focused on identifying and clarifying the purpose of MYPs and developing key indicators to guide country decision-making. These meetings obtained countries' perspectives and experiences on how they prioritize hotspots for OCV, examined selection criteria, discussed thresholds and guidance for countries, and sought and obtained feedback on the proposed criteria from the larger OCV working group.

The sub working group identified four main categories of indicators: the susceptibility of the population (e.g., as measured by previous OCV campaigns, recent cholera reported); the risk of transmission or spread (e.g., population density, risk of importation and/or cross border transmission); the vulnerability of the population (e.g., the presence of high-risk populations, unusual weather patterns, etc.); and operational considerations (e.g., accessibility, seasonality, etc.).

The next step in this process will be to review how to combine this prioritization tool with the hotspot identification tool, particularly the vulnerable criteria in the hotspot identification tool, then to pilot it in several countries to support MYP development.

Training to strengthen country capacity to request and use OCV

This project was a partnership between WHO, Gavi, MSF, US CDC, the International Federation of Red Cross and Red Crescent societies (IFRC), UNICEF and MMGH Global Health Consulting to design a workshop addressing challenges with the quality of applications, increase campaign quality, and increase general knowledge about OCV and campaign implementation. The workshops were designed to build practical skills on developing emergency and preventative OCV campaign requests; train recipients to identify which areas in an active outbreak should be targeted with OCV, and how to identify hotspots to prevent cholera outbreaks; and to improve knowledge of the essential components of planning, implementing, and monitoring campaigns.

The first multi-national five-day workshop took place in Nigeria in April 2022 for MOH staff, GTFCC partners and consultants who would be part of OCV decision-making. Representatives from six countries received the training: Ethiopia, Kenya, Mozambique, Nigeria, South Sudan and Uganda. The course was well received, with several attendees commenting that they would use what they learned when they returned home, either to develop or finalize their NCP, or when drafting an OCV request. WHO has also since received anecdotal reports of improvements in OCV requests, and the WHO OCV Focal Point has indicated not only that requests received from workshop attendees have been of high quality, but also that new countries have since submitted requests. Colleagues in the room backed up these positive reports, with comments from the floor emphasizing that the workshop had helped focus on outbreaks, improved NCP development and evaluation, facilitated connections with colleagues from neighbouring countries, enabled cascading of training at home, and boosted MYP development.

The next steps in this project are as follows:

- Conduct training for francophone African countries (in DRC in October 2022)
- Conduct training for countries in Asia (Q2 2023)
- Conduct sub-national trainings (in Ethiopia in November 2022)
- Produce an online version of existing training
- Develop indicators to track and document the impact of the training.

OCV campaign readiness assessment tool

US CDC and WHO are working on an OCV campaign readiness assessment tool for countries preparing preventive campaigns, with the aim of supporting higher-quality planning and implementation of national campaigns. The development team reviewed other disease-specific assessment tools and country campaign reports before deciding to base the new tool on the framework of an existing measles supplementary immunization activities (SIA) readiness assessment tool. This resulted in an adaptable, Excel-based tool containing a categorised list of priority activities, sorted into national and subnational levels, with timelines for completion and implementation. The tool advises national authorities to begin preparation nine months before the start of a campaign, and subnational authorities to begin six months before. The tool can also be used as checklist and as a reporting tool and will be accompanied by an implementation manual.

Development was in its early stages at the time of the meeting: a prototype had been circulated to technical and country partners, and feedback was being incorporated. The team's aim was to pilot the tool in a minimum of two or three countries in the 12-24 months after the meeting. Any countries planning preventive campaigns are invited to contact the working group to discuss its use.

OCV allocation framework for fair shipments

Work on a transparent and fair process to prioritize OCV shipments in supply constrained situations should start work in Q4 2022. A sub-working group will be convened in 2023 to develop an allocation framework as has been done for other supply constrained vaccines e.g., COVID-19 and malaria.

OCV dashboard

After a short demonstration of a data sharing dashboard, a round of discussion raised a few points.

- There was some concern about how challenging it will be for countries to update the dashboard regularly. The dashboard presented in the meeting is already available and contains all district level data entered up to the end of 2020, with two years of data still remaining to collect. It is

expected that gathering district-level information will be challenging. A tool has been produced to support data import.

- The capacity to download information from the dashboard was widely appreciated and is expected to be a great help to countries' planning processes.
- The most challenging part of the tool is the geo-matching and integration of GIS. But this has been done for other outbreaks, so a proof of concept exists.
- Automation and automated checks would be a useful addition – for example, prepopulation of relevant fields when doses are sent to countries; prompts for incorrect values; "something in an easier format to avoid errors;" and additional checks to confirm data is correct. There was agreement that the dashboard may require a more careful validation system that incorporates human supervision.
- The ability to export information in same format as that which is required for ICG requests would be hugely valuable. If the data are there, that should be possible.
- There was discussion of whether it would be possible to have automatic pulling of data into the tool – for example, shipment information – to make it more effective in real time. The technical team acknowledged that automatic pulling would be desirable, but practical considerations mean it is likely to remain manual.
- Before data goes live it should be verified with UNICEF – there have been many occasions in the past where there have been discrepancies in the numbers of doses shipped and the dates.
- There was also discussion of whether a similar effort is likely to be made with surveillance data. An effort is already underway to have a global section on surveillance data containing variables related to case numbers, locations, confirmation status, etc., but the entire dataset is not yet defined. This task is difficult because it involves a lot more data – and more sensitive data – than for vaccines. This functionality is coming but is unlikely to arrive soon.
- The historical data is already in the GTFCC database; the current gap is around up-to-date, real-time data. There has been some talk about the use of short-term tools to ease data entry for line lists and sitreps to allow tracking outbreaks closer to real time. Discussions are ongoing within the surveillance working group about the longer-term future of the database in the GTFCC when the focus is increasingly on real time data. Approaches and tools are in an interim phase.
- The ICG also has a dashboard.
- A request was made to consider the ability to export and import data between this tool and the ICG dashboard. This interoperability is possible, but the export options depend on the dashboard. The indicators and figures would have to be the same "or chaos would result."

Discussion on activities for 2023

Ms Bouhenia presented the following new activities under consideration for 2023:

- Guidance
    - Develop guidelines for allocation of OCV for preventive campaigns among countries
    - Support revision of ICG guidelines on reactive use of OCV
- Operations
    - Develop an online version of the request/campaign workshop
    - Review campaign evaluation and integration tools
    - Develop a webinar to build awareness of the new OCV request process through Gavi
    - Develop an OCV strategy.

There was then an open call for country and partner ideas on proposed activities, resulting in the following suggested activities:

- Revision of ICG guidelines for reactive campaigns
- Development of an MYP orientation, to give countries more detailed understanding of how to make and implement a five-year plan
- Acceleration of planned trainings and online trainings so all countries are ready for MYPs
- Development of guidance on what transition from Gavi support will mean
- Work on how to improve demand forecasting for preventive campaigns (for example, in 2024 alone Bangladesh is likely to need more doses than the entire available supply)
- Continue discussions around future vaccines to keep the development pipeline moving, determining where future vaccines will fit and what the market might look like
- Once a new roadmap is available, coordination of messaging to countries
- Work to solidify demand and ensure that countries are not self-limiting their requests in response to vaccine supply constraints, but fully expressing demand so that manufacturers understand their needs
- Assessing the feasibility of incoming demand projections. Much has been said about single countries needing 100m doses over the next few years, but the experience of other preventive campaigns – for yellow fever and meningitis, for instance – show that no matter how ambitious countries are to do massive campaigns quickly, feasibility is low.
- All GTFCC guidelines and tools should be translated as quickly as possible. Some WHO tools are currently only available in English.

After the repeated calls for more and better forecasting, the meeting was reminded that Gavi has been working on its newest strategic demand scenarios, with an updated roadmap to be published this year.

Progress on OCV research priorities

The Research Agenda launched in early 2021 at the start of a longer-term effort to identify and prioritize research questions, attract donor funds, and encourage links between research and implementation. Its goal is a situation in which research and evidence address the needs of people implementing the Cholera Roadmap and the populations most affected by the disease, with the efforts and resources of the cholera control community aligned to answer the most pressing research questions and encourage discovery, research and innovation, creating more effective tools and strategies and a stronger evidence base to accelerate progress towards the Roadmap goals.

The agenda identifies 20 research priorities across the pillars, with nine related only to OCV and two more cross-cutting and including OCV (Figure 4).

Figure 3: GTFCC research agenda priorities

PILLARS	ORAL CHOLERA VACCINE	WATER, SANITATION & HYGIENE	SURVEILLANCE	COMMUNITY ENGAGEMENT	CASE MANAGEMENT	ALL PILLARS
RANK OVERALL	PILLAR	RESEARCH QUESTION				
1		What are the optimal oral cholera vaccine schedules (number of doses and dosing intervals) to enhance immune response and clinical effectiveness in children 1 to 5 years of age?				
2		What are potential delivery strategies to optimise oral cholera vaccine coverage in hard-to-reach populations (including during humanitarian emergencies and areas of insecurity)?				
3		Is there additional benefit to adding WASH packages, for example household WASH kits, to an oral cholera vaccine campaign?				
4		What is the optimal number of doses of oral cholera vaccine to be used for follow up campaigns in communities previously vaccinated with a 2-dose schedule?				
5		Can the impact of oral cholera vaccine on disease transmission, morbidity and mortality be maximized by targeting specific populations and/or targeted delivery strategies?				
6		What are the barriers and enablers for integrating cholera treatment into community case management by community health workers?				
7		What levels of coverage for relevant water, sanitation and hygiene interventions is required in cholera hotspots to control and ultimately eliminate the risk of cholera?				
8		What impact does the timing of oral cholera vaccine use have on outbreak prevention and control?				
9		What is the impact of early diagnosis of cholera using a rapid diagnostic test at the point of care in a community setting compared to testing only in health facilities?				
10		How can the use of oral cholera vaccine in the controlled temperature chain (i.e., outside the cold chain) be leveraged to maximize the coverage or impact of vaccination in a field setting?				
11		What is the incremental benefit of implementing a comprehensive interventions package (including water, sanitation and hygiene, antibiotics, oral cholera vaccine, oral rehydration therapy) to reduce cholera mortality during an epidemic?				
12		What is the effectiveness and impact of different vaccination strategies for rapid response to cholera outbreaks (e.g., ring vaccination, case-area targeted interventions, etc.)?				
13		What is the most cost-effective package of water, sanitation and hygiene, and oral cholera vaccine in different situations, based on transmission dynamics in cholera hotspots?				
14		What are the most essential (or what is the minimum set of) infection, prevention and control (IPC) interventions in cholera treatment facilities and oral rehydration points to reduce risk of transmission within these facilities?				
15		Are there immunisation strategies other than repeated mass campaigns that will be effective in preventing endemic or epidemic cholera?				
16		What is the role and added value of CORTs (community outbreak response teams) in enhancing case investigation and outbreak detection?				
17		Can oral cholera vaccine be co-administered safely and without interference with other vaccines during mass campaigns or during routine immunization visits (measles containing vaccines, yellow fever, typhoid, meningitis, pneumococcal conjugate vaccine)?				
18		What are effective strategies to scale up the use of household water treatment in controlling cholera outbreaks?				
19		How can we improve and fine-tune hotspot definition and identification at a district and sub-district level, such as micro-hotspots?				
20		Is improved access to safe water (e.g., water points and distribution networks) effective in controlling and preventing cholera outbreaks?				

■ Cross-cutting Research Priorities which involve more than one pillar

The top five OCV research questions pertain to use –

1. What are the optimal OCV schedules (number of doses and dosing intervals) to enhance immune response and clinical effectiveness in children 1 to 5 years of age?
2. What are potential delivery strategies to optimize OCV coverage in hard-to-reach populations (including during humanitarian emergencies and areas of insecurity)?
3. Is there additional benefit of adding WASH packages, for example household WASH kits, to an OCV campaign?
4. What is the optimal number of doses of OCV to be used for follow-up campaigns in communities previously vaccinated with a two-dose schedule?

5. Can the impact of OCV on disease transmission, morbidity and mortality be maximized by targeting specific populations and/or targeted delivery strategies?

– with an additional discovery priority being "the discovery and development of new and improved vaccines."

25 cholera vaccine-related projects are listed in the Cholera Research Tracker database – many of which were initiated prior to development of the research agenda – and six research projects are currently identified as active in the tracker. This does not represent all ongoing research, and any participants active in research are reminded to update their project status (and/or add new projects) in the tracker.

Of these six active projects, based on the title and/or short description included in the database, three correspond to question 5 in the list above, "Can the impact of OCV on disease transmission, morbidity and mortality be maximized by targeting specific populations and/or targeted delivery strategies?" These are the impact of mass cholera vaccination in Uvira, Democratic Republic of the Congo (Johns Hopkins University (JHU), DRC); Impact evaluation of OCV preventive campaigns (Epicentre, DRC); and Ethiopia Cholera Control and Prevention (ECCP) (International Vaccine Institute (IVI), Ethiopia). The other three relate to the discovery goal: OCV reformulation (IVI, South Korea); O-specific polysaccharide responses and cholera (Harvard University and Massachusetts General Hospital, USA); and development of a rapidly active live-attenuated cholera vaccine (Brigham & Women's Hospital, USA).

Gaps and priorities for future research identified in the 2021 meeting included work on dose intervals and the use of antibiotics in case area targeted interventions (CATIs) in response to outbreaks, neither of which has any active projects yet listed in the tracker; and new vaccines, for which there are the three active projects specified above.

Updates from OCV researchers

International Vaccine institute (IVI)

Work on a simplified OCV formulation in conjunction with Eubiologics is nearing the end of the Phase 3 trial, with results expected in Q1 of 2023. If successful, this research will improve production capacity at Eubiologics (see Euvichol-Plus production update below).

A new project is in preparation, in partnership with Wellcome, on a capsule OCV most easily described as "Dukoral in a capsule." GMP manufacture and a Phase 1 trial are planned for 2023.

Work on a new conjugate vaccine was ready to start a phase 1 trial the week after the meeting. The development effort required means the world is probably still 7-10 years away from a usable conjugate vaccine, but this is a promising project. Such a vaccine would be a very different tool to those that currently exist.

Johns Hopkins University (JHU)

JHU has an ongoing study in partnership with the London School of Hygiene and Tropical Medicine (LSHTM), the DRC Ministry of Health and the University of Utah on impact of OCV campaigns on clinical incidence and seroincidence. The research campaign was conducted a few years ago and the team has followed up cases and done systematic testing, completing a serosurvey and a population representative survey to track evolving coverage. Estimates of the short-term effectiveness of Euvichol-Plus will be available in the 6-8 months, along with estimates of the impact on incidence of this campaign and the probable impact of combining OCV campaigns and other cholera control activities.

University of Gothenburg

The capsule vaccine mentioned in the IVI update above has just finished a clinical trial.

International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b)

icddr,b has an ongoing study on the use of antibiotics.

Epicentre

An Epicentre CATI trial is outlined in a poster in Annex 1. The trial looked at targeted interventions within a multi-intervention package, and results are promising, suggesting this method can be reactive, allowing vaccination within about five days, with very few secondary RDT+ cases reported.

Recruitment has started (after a slight delay) for a study on dosing schedules.

A Wellcome-funded OCV impact study in Goma, DRC is ongoing, in partnership with JHU. This study will be based on five years' detailed surveillance in all cholera facilities in rural and urban sites and is currently a year into surveillance, with several serosurveys completed. The analysis step will determine the number of infections. Goma had an OCV campaign in 2019/20, and the study is tracking the subsequent evolution of incidence and household transmission.

Bill and Melinda Gated Foundation

The Foundation is involved in several of the studies mentioned above, as well as an OCV effectiveness study in Bangladesh run in partnership with icddr,b and US CDC.

Wellcome

Most cholera studies in which Wellcome is involved are already detailed above, but in 2023 Wellcome would also like to launch a funding call on cholera research uptake, addressing priorities for the research agenda and the roadmap. Details are still to be confirmed.

DRC

DRC is seeking partners to help assess the efficiency of the national cholera response. In 2019 and 2022 DRC tested certain strategies (CATIs, the GRID approach, etc.) and is running a study to clarify the results generated from each.

Discussion

A brief period of discussion about the research priorities for 2023 raised a few important points.

- There is a need to address two key policy questions for Euvichol:
    - Firstly, the WHO position paper recommends OCV for pregnant women, but this is contrary to manufacturers' recommendations and causes confusion in countries. Clearer guidance is needed. Changing pregnancy guidelines on manufacturers' recommendations will mean changing packaging inserts and going through the Korean MOH, but there is insufficient data currently to support this so it cannot be done at this stage.
    - Secondly, regarding thermostability, a study on Shanchol suggested that the vaccine regained immunogenicity at around 43º. In absence of data, it is impossible to be confident about thermostability, and cold chain challenges are rife. On thermostability, a simplified Euvichol vaccine (Euvichol-S, see Eubiologics update below) will be more thermostable, as it does not contain O139. Research to generate the missing data could be done if that data is needed.
- On thermostability and OCV in general, it would be useful to have better data on the use of OCV in CTC conditions, given the usefulness of this approach in reaching remote populations. More information on CTC research can be found in the poster in Annex 1. Eubiologics is in discussion with WHO about CTC prequalification (PQ) for Euvichol-S. If all goes well, CTC PQ is expected by the end of 2023.
- Another important evidence gap is the duration of protection against cholera following OCV receipt, particularly effectiveness studies. There is strong data on three-year individual

protection, with weaker data (based on one study) on five-year protection. GTFCC and country decision-making would benefit from better understanding what happens in the field as opposed to in randomized control trials (RCTs). With the accumulated experience of having administered over 100m doses, it should now be possible to say more about periodicity and anticipation of the need for revaccination. Haiti is one place from which this evidence might come, following up on case control studies done 8-9 years ago.

- A research coordinator for the country support platform was being interviewed at the time of the meeting.
- The research tracker is a good tool to improve research communication to the working group, but only if people get better at updating it. Completed projects are still listed and visible on the website with their proposals, and flagged as completed, but with no accessible follow up to recommendations, outcomes, published studies or anything else. It would be a welcome improvement to have full links to outcomes rather than just the 'completed' marker.
- The plan after the 2021 meeting was to include research updates in working group calls. While this has not been possible in the last year, it remains an ambition to invite researchers working on specific topics to present their research on these regular calls. Direct communication is likely to increase next year.
- There was consensus on the following emergent themes for research:
    - Thermostability and CTC;
    - safety of OCV among pregnant women;
    - duration of protection; and
    - the potential of useful data from Haiti to inform on longer term duration of protection.

Opening of the funding window for preventive use & progress in the OCV Market Shaping Roadmap

Allyson Russel *and* ***Olivia Bullock****, Gavi*

Launch of the new preventive programme

The new situation around Gavi support for OCV is summarised in Figure 5.

Figure 4: Gavi support for OCV

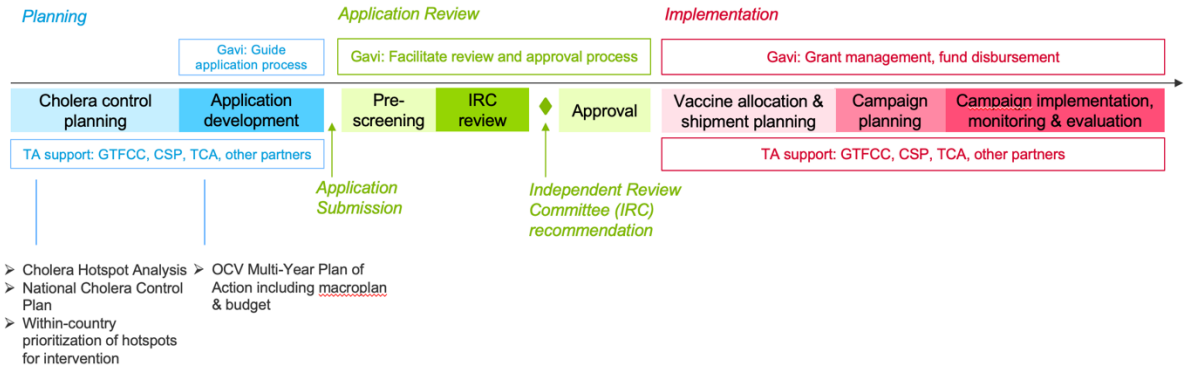
	Vaccine support	Financial support	Programmatic guidance
Preventive Use in Hotspots (Funding available from Jan. 2023 directly from Gavi)	Doses **fully financed** by Gavi Repeated use in short time interval may be subject to co-financing	**Operational cost support** provided by Gavi, with ceiling based on country transition status **Targeted Country Assistance** & **Health Systems Strengthening** funds	Multi-year phased campaign plans in cholera hotspots Annual dose allocation & planning cycle High 2-dose coverage required
Emergency Response (via ICG)	Doses **fully financed** by Gavi	**Operational cost support** provided by Gavi via WHO to facilitate rapid implementation	One time emergency campaigns in areas with confirmed outbreak or pre-emptive vaccination High importance of rapid implementation of 1st dose

The transition timeline to the new support model is as follows:

- Q3 2022: OCV funding guidelines released
- Q4 2022: Transition period begins (country and partner training and orientations, application development for GTFCC-approved plans); 2023 allocation (contingent on completion of allocation framework)
- Q1 2023: Gavi funding window opens for multi-year preventive OCV campaign applications
- 2023 (ongoing): continuation of preventive campaigns approved by GTFCC in prior years; new applications approved and processed via Gavi
- Q4 2023: Preventive campaigns approved by Gavi begin to be implemented.

The respective roles of Gavi and other partners in the application, review and disbursement processes are explained in Figure 6.

Figure 5: New process for preventive campaign planning, application and implementation



Elements of the new application include a workplan with a high-level activity timeline, budget, and targeted areas; more detailed budgeting; and vaccine specific documents including the MYP, a hotspot analysis report, the NCP, reports from recent campaigns and endorsements. Of these, the MYP is the key document. The NCP, while only ”strongly recommended” for the first submission, will be a requirement for re-vaccination applications.

Despite current supply issues, countries are encouraged to engage with this new process and make applications. While the short term OCV supply situation is bleak, the importance of the MYP is that it addresses the longer term, establishing OCV demand over multiple years. Gavi is working on an analysis

of supply projections that should establish confidence in longer-term supply; this should be available by the end of the year.

Countries will receive guidance as they develop their application plans, with the GTFCC OCV focal point, the CSP team and Gavi team providing support. Key considerations for planning these applications include the following:

- Vaccination plans must be based on GTFCC-endorsed hotspot analysis
- The NCP is strongly recommended for a first application and will be obligatory for re-vaccination applications
- Multi-year plans mean only one application needs to be made per MYP period (modified annually if needed)
- There will be no co-financing of doses unless there are multiple campaigns in a short time in the same location
- Operational costs are tiered based on country transition status
- The allocation process will determine the doses that countries should expect each year
- Integration into national immunization strategies, health sector plans and other Gavi funding mechanisms is strongly encouraged
- It is expected that countries will identify and exploit opportunities to leverage campaigns to identify and reach communities that need other health interventions (vaccines, medicines, commodities etc.).

Market shaping roadmap

Gavi's market shaping roadmap will be published by the end of 2022. Its goals are to optimize short-term supply, meet mid-term demand and secure a sustainable long-term supplier base, improving the materialization, predictability and quality of preventative OCV programmes and ensuring continued availability of appropriate and innovative vaccines. This plan was developed on the back of a market analysis that included demand and supply analysis and the development of a "healthy markets framework," and an objective prioritization process that generated seven target outcomes.

Discussion

- Further information on co-financing is laid out in a Gavi document called *Vaccine funding guidelines*. All countries are expected to follow SAGE recommendations (i.e., vaccination no more frequently than every three years unless there are serious extenuating circumstances). Plans to vaccinate at shorter intervals are a signal that something unexpected is happening and co-financing might be considered under these circumstances.
- Throughout the transition phase, any country in the middle of an existing Gavi agreement remains eligible to complete their campaigns.
- The guidelines clarify that OCV is expected to be part of a broader response that includes WASH.
- Under this new model the GTFCC remains responsible for guidance and support to countries for cholera control planning, hotspot analysis, determining where to vaccinate, etc. – all of which take place in the planning phase. Once these plans and analyses are in place, the GTFCC will provide an initial review of the country's application before it is submitted to an independent review panel at Gavi, which then provides Gavi with a recommendation to approve. Overall planning approaches will not change. The key document in this process is the MYP, a model that has been extensively informed by GTFCC working group advice.
- Even in a very good scenario for 2023 only around 10m doses will be available for prevention in all countries. This must be handled carefully when engaging countries on MYPs. In the longer term, projection from market analysis and the roadmap will be useful for countries. Other

companies are expected to enter the OCV market in the near future. Countries should be thinking about MYPs that start implementation in 2024, but the process to develop those plans will be challenging.

Euvichol-Plus production update

***Rachel Park**, Eubiologics*

At the time of the meeting, 4 648 650 doses of Euvichol-Plus were ready for shipment, with 10 277 500 doses expected to be ready by the end of 2022. In 2023, 36 million doses will be available for shipment.

EuBiologics has been working on a second site to double production capacity. This additional site is expected to be prequalified in March 2024. It will also contain an additional fill/finish facility to increase the capacity (and as a contingency plan for the first site) that will be completed by June 30 2024.

Euvichol-S

Eubiologics is working on a simplified formula for Euvichol. The current OCV contains five components: redundant heat and formalin inactivated O1 Inaba and Ogawa and Vibrio cholera O139. The new formulation, Euvichol-S, is a simplified formulation containing only two current components (O1 Inaba (El Tor) and O1 Ogawa (classical)), inactivated by a single method. If found to be equally effective as Euvichol-Plus, this could lead to production cost reductions and an increase in production capacity of around 35%.

A phase III, multi-centre, observer-blinded, randomized, active controlled trial to evaluate immune non-inferiority, safety and lot-to-lot consistency of Euvichol-simplified (Euvichol-S) vaccine as compared to Shanchol in healthy patients aged one to 40 years is now ongoing in four sites in Nepal. Non-inferiority of Euvichol-S compared to Shanchol is measured by seroconversion rates of anti-V. cholerae O1 Inaba and anti-V. cholerae O1 Ogawa vibriocidal titer two weeks after second doses of vaccine for all ages. 2530 subjects are enrolled in the study and results are expected at the beginning of 2023.

Euvichol-S is expected to be prequalified by the end of 2023 at the earliest, if concurrent review by the Korean Ministry of Food and Drug Safety and WHO PQ is feasible. If concurrent review is not feasible, prequalification is expected by the end of 2024. EuBiologics has already engaged with WHO PQ to discuss this. Concurrent review of Euvichol-S PQ and CTC is also anticipated.

On future production capacity, if there is sufficient demand, EuBiologics will consider hiring drug product contract manufacturing organization (CMO) in 2024 and 2025.

Dr Park then laid out possible levels of future production capacity depending on whether this decision is taken and whether the company is producing Euvichol-Plus or Euvichol-S – only one will be produced, not both (Figure 7).

Figure 6: future production capacity for Euvichol

		2024	2025	Note
Euvichol-Plus	DS	58	65	Currently 33md, increasing 65md by April 2024 when 2nd site is online
	DP	41	70	Currently 41md capacity, increasing 91md by June 2025 when 2nd site is online
Euvichol-S	DS	80	80	Assuming a 38% increase in antigen availability following PQ of Euvichol-S in Sep 2023 earliest (based on concurrent review). However, we assume that we switch from Euvichol-P to Euvichol-S from 2024.
	DP	41	70	Currently 41md capacity, increasing 91md by June 2025 when 2nd site is online

<Max availability of OCV from EuBiologics>

(Unit: Mil)	2023	2024*	2025~
Euvichol-P	36	58	65
Euvichol-S	NA	80	80

*In 2024, EuBiologics can consider DP CMO for either glass vial or plastic tube if demand picks up.
**DS capacity: Assuming 33M in the 1st site and 25M in the 2nd site.

Discussion

- The levels of future production capacity presented are theoretical maximums if no problems occur, and could be lower. But Eubiologics has been making Euvichol-Plus for years with a very good production history and Euvichol-S is an even simpler process, so problems are not expected.
- National regulatory aspects continue to raise problems. Euvichol-Plus is registered in over 10 countries including Mozambique, Zambia and Nigeria, but growing that list is difficult. The biggest challenge is identifying local agents to register it because OCV has such limited private market potential.
- To justify scaling up production further, Eubiologics would need not only Gavi forecasts and UNICEF requests but also – given the volatility of demand – assurance that there will be enough demand. Engaging with drug product CMO would require serious investment, and advance payment from UNICEF might be required to increase production beyond what can be done in-house.
- Gavi supply & demand scenarios (SDS) could be linked to supply projections. They are key projects for supply/capacity decision-making, so this is an important area; but it would take a lot of time and effort.

Allocation framework for preventive OCV use

This session was designed to showcase experiences from other supply constrained vaccines programs.

Malaria: developing a framework for allocating limited malaria vaccine supply

***Eliane Furrer**, WHO Malaria Vaccine Team*

WHO provided recommendations for use of the first malaria vaccine in October 2021, recommending that the RTS,S/AS01 malaria vaccine be used for the prevention of *P. falciparum* malaria in children in regions with moderate to high transmission. This injectable (intramuscular) follows a four-dose schedule, starting in children from five months of age.

As with cholera, vaccine supply will be insufficient to meet demand in the coming years. Over 25 million children are born each year in regions with medium to high malaria transmission and potential peak demand could be 80m – 100m million doses per year, but currently only 18 million doses will be available between 2023 and 2025. Around one third of the available supply is committed to Ghana, Kenya, and Malawi where the vaccine has been piloted.

WHO has therefore developed a framework for allocating this limited supply. To contextualise discussion of the framework Dr Furrier quoted an extract from the considerations of the WHO Working Group on Ethics and COVID-19, *Ethical foundations of a global vaccine allocation framework for COVID-19:*

> Out of the many ways that we might choose to allocate scarce resources, this choice represents the objective that is being valued most…Science and/or evidence alone cannot tell us which choice or aim is 'correct' or which aim society should value most. This requires a value judgement, which is the domain of ethics… Consequently, the first step in developing a framework for the allocation of scarce resources requires explicit consideration and clarification of ethical values—values that technical considerations and mechanisms should subsequently operationalize… It is equally important to morally justify who is to make these decisions.

The purpose of the malaria Framework is to offer global guidance on the allocation of RTS,S/AS01 and other malaria vaccines as they become available, and on prioritization of areas for vaccination within countries until supply constraints can be resolved. The intended audience is policymakers in endemic countries, the manufacturer(s), Gavi, and other funding, implementing and technical partners. The Framework is meant to be dynamic to support prioritization at the start of vaccine roll-out and over time as supply increases. In-country deployments should respect sovereign decision-making and align with the High Burden to High Impact approach to sub-national tailoring of malaria interventions.

Dr Furrier laid out the framework development process in detail, highlighting the transparent system for classifying levels of need and how the fact that some countries (DRC, for example) have very high needs that could potentially use up all of the supply led to the inclusion of a solidarity principle/cap. This cap states that "initially, if there are unmet vaccine requests for greatest need areas across multiple countries, no single country should receive more than 20% of total available supply." The initial cap is 1 million doses per year.

Key implications of this framework for countries are as follows:

- No country is excluded by the framework
- All countries will have to consider a phased approach to vaccine implementation, starting in areas with highest need, with expansion after supply increases
- The framework clarifies allocation principles, but some uncertainties remain:
    - there are no fixed vaccine quantities set aside for each country;
    - need is stratified based on country-specific data;
    - applications are first reviewed by Gavi's Independent Review Committee (IRC);
    - interest from other countries remains unclear; and
    - the timing of future increases in supply is uncertain.

To manage expectations and support planning, countries will be engaged in individual discussion about potential initial allocations.

In conclusion, there is no single "best" or "true" solution to supply constraint for essential vaccines. To address such a difficult ethical situation the process through which any prioritization mechanism is developed is as important as the eventual nature of the mechanism itself. Acceptance and adherence by all key stakeholders – countries and communities, manufacturers, funders, implementing partners, etc. – is key to success. A dynamic mechanism is needed to deal with changes of supply and demand dynamics over time, and throughout development and implementation transparency and communication are essential.

Discussion

- Like cholera, malaria provokes discussions about equity versus burden and the difficulty – and unfairness – of setting thresholds. The malaria team addressed this by making their first principle to reach those most in need, with maximizing health impact a second priority. There is inevitable tension: for example, maximising impact might target areas with greater potential for higher coverage, but that often favours better-off areas. Many members of the Expert Group have personal experience of this tension, having grown up in areas neglected by new interventions because decision makers never prioritize them because they know coverage will be poor. The team felt it important to address the highest need and not to reinforce structural injustices. This approach is more challenging but hopefully also provides impetus for integration and access.
- The GTFCC has a very active vaccine working group that is an excellent platform for discussion and can learn a lot from this experience in developing the framework for OCV allocation. The GTFCC setup has a high number of development partners involved and should make it easy to develop a framework in a participatory way.
- A further similarity between the situations for malaria and cholera is the fact that the vaccines are not the only effective prevention measures. Applications for malaria vaccine must describe how the vaccine is integrated into malaria control, and countries are encouraged to develop an addendum to their control strategy as part of the application. Allocation does not, however, consider coverage of other interventions, because that would add other inequities.
- There was brief discussion of whether and how the Working Group should address allocation principles. It would be a good forum to initiate discussion, but one of the principal strengths of the malaria approach was the breadth of the process, and how it encompassed all partners. That broader input (and thence buy-in) is extremely valuable in the longer term. Principles for a similar framework for cholera were presented at the working group some years ago, and it would be worth reflecting on what happened to them.
- For cholera, uncertainty around preventive allocation is unavoidable. An equivalent cholera framework would have to address issues raised by the needs for both reactive and preventive doses, because big outbreaks would overrule the framework. It would have to be designed with the flexibility to cope with this and accompanied with guiding principles for the ICG.

The chair asked for an informal show of hands as to whether the working group would like to commit to a similar process of addressing allocation principles, particularly given that it might be helpful through the coming period of supply constraint.

There was a slight majority of Yes votes.

Allocation framework and hotspot identification

A new allocation framework would greatly affect the design and implementation of preventive campaigns, especially if more countries are doing hotspot analysis and developing MYPs. It would be valuable to agree principles to help countries implement those plans in a fair and appropriate manner. There was a quick

discussion of the challenges that countries face when working to identify hotspots and take the other steps required to access OCV. These challenges, if identified well, form the backbone to any new prioritisation and allocation principles.

- **Ethiopia** struggled to obtain five-year data. When data was processed, the output was of poor quality because it excluded some woredas affected by outbreaks. Obtaining data that enabled authorities to build up the real picture on the ground was the hardest part.
- **DRC** has a lot of mapping experience using epidemiological surveillance data, but wanted to integrate mortality and lab data, especially given that the latter is crucial for confirmation. This data was unavailable in some parts of country, a problem exacerbated by reduced access to labs in some health zones. This meant that deficiencies in the lab indicator had to be accounted for in the hotspot analysis.
- In **Somalia**, hotspot mapping in 2017 enabled the cholera strategy and the five-year response plan. These need to be updated and should improve as the surveillance system has been strengthened and data for projections is now more reliable. A review of the national response will be done to update the mapping.
- **Benin** did not face any notable problems but was assisted with hotspot mapping by a WHO consultant. Data was available back to 2016, allowing the identification of 15 hotspot districts in seven of 12 regions.
- **Zambia** wanted to use WASH data to strengthen mapping, but the data was unavailable at the levels required. The decision was taken to complement incidence/persistence with WASH data in the narrative sections instead. This process did help identify new hotspots and assisted the NCP review.
- Micromapping of data at a very granular level is important for hotspot mapping, but also crucial to the Gavi SDS at global level. Many countries do not have data at this level, and the GTFCC and others must consider surveillance and other aspects when designing tools. Simple approaches are the best way to provide support to countries. It is encouraging that so many countries feel like hotspot identification is now feasible.
- Work is ongoing to present the data that do exist to build as accurate a view of existing cholera as possible. The focus to date has been on Africa, and on creating a base map for hotspots that can be used in situations where granular official data do not exist, but where there may be line lists from partners or other things that contribute to the picture. There are uncertainties and issues with all this data, but if it is averaged out to create the best possible maps, that can be helpful. A new round of such maps should be available in the next few months. They do not replace the in-depth, context-based hotspot investigations that ministries can do, but they provide a useful base from which to work in the absence of something better.
- Countries were reminded that the GTFCC is a resource for hotspot mapping, and that they should ask for any support they might need.

OCV implementation priorities: integration of other activities

The session started with brief presentations by countries of their experiences of integrating OCV with other activities, and the challenges they faced.

Mozambique

During Cyclone Idai, OCV was integrated with bednet distribution. The first round “was a complete disaster” because service delivery for the two activities was planned separately. Learning from this, the

second round was better, but things improved most when it was not just activities that were integrated, but money as well. If the money is not integrated, only limited success can be achieved, because each funding source will have its own indicators and milestones. For example, bednet distribution favours fast delivery to as many people as possible, but OCV needs to be delivered accurately to known persons, with their health data checked. If these considerations are not in the microplanning of the health services agencies, problems arise.

Another campaign was done at the start of conflict in northern Mozambique, integrating OCV with WASH delivery by humanitarian organizations in refugee camps, but the movement of the people and the conflicting priorities of the humanitarian organizations involved meant that the vaccination was relatively unsuccessful. On the other hand, the WASH interventions – water, education, sanitation and latrine provision – were very successful.

DRC

DRC integrates OCV with the distribution of WASH kits including water treatment and soap, the need for which is identified in the pre-vaccination phase of the OCV campaign. These kits are available in public places, schools and churches, especially during outbreak periods. Vaccination teams also contain food safety and mobilization and sensitization components. A central challenge has been the lack of enough trained staff to carry out all these functions properly during a vaccination campaign.

Experience has also shown that integrating WASH also improves acceptability of, and adherence to, OCV. Communities tend to know that cholera comes from untreated water, so vaccination teams take the opportunity offered by the OCV campaign to do door-to-door distribution of WASH kits (including water treatment tablets) and messaging. In the past, failure to cost for this has resulted in the need to mobilize partners, disrupting the smooth running of campaigns.

Kenya

The main challenge of integration is the need to move away from total focus on immunization and towards nutrition, deworming, WASH, etc. – all areas with different, sometimes competing priorities. On a practical level, this means that integrated campaigns can be affected by extrinsic availability issues (e.g., the cholera programme might be ready with OCV, but the nutrition programme has not yet secured vitamin A, so an integrated campaign cannot start) and logistical problems (e.g., mobility issues – if the OCV teams travel on motorbikes but now include additional people, WASH equipment, etc. that poses serious challenges). Kenya has made the decision not to integrate immediate campaigns because it would be too difficult but will keep the possibility open in the longer term.

Nepal

Nepal has integrated OCV with WASH messaging since 2016. Hygiene promotion messaging is run alongside immunization sessions, with community health volunteers displaying different items so people can learn about hygiene practices. This imposes additional costs. Attempts to integrate OCV with the work of other teams – including vitamin A, deworming and other campaigns – has been less successful, because those sectors have conflicting priorities and schedules. Multisectoral work is hard: "'integration' is a beautiful word, but a challenge in the field."

Somalia

Collaboration is always an issue – and not only with partners, but also within large organizations like WHO and UNICEF. Somalia has learnt to involve everybody in microplanning for integrated projects, and to support committed workers in different locations around the country who spread messages to create demand. OCV campaigns are a beehive of activity by different sectors, the success of which is dependent on how different teams are included in planning. The process involves everybody, including when agreeing dates, because there is a need to identify the windows in which different teams can provide their packages – for example, so WASH teams can plan kit distribution alongside OCV campaign schedules. To increase accountability and involvement, Somalia also holds after action reviews for OCV campaigns in which every sector reports based on its targets and outputs.

Ethiopia

Ethiopia has not yet done any preventive campaigns, but in small scale reactive campaigns short term WASH interventions have been done alongside OCV. The usual problem is one of coordination: if that is addressed and programmes are implemented well, integration is cost- and resource-effective. In the past an integrated deworming campaign was dropped because it decreased OCV uptake, suggesting that success depends on what is integrated and how. Some integrations will be positive – for example, WASH increases OCV coverage if people come for WASH supplies – and some negative. Better understanding of context is needed to know what effect a particular integration will have.

Uganda

Uganda compiles data at end of each campaign and depending on the gaps it reveals, plans are made with partners to support activities in response. Vaccination teams move house to house and include health education and WASH messaging, but otherwise short-term WASH is not supported during campaigns. Uganda takes a longer-term view on WASH, using OCV campaigns to collect data and gather WASH indicators.

Niger

In Niger, integration is done through containers that provide WASH facilities, which were put in place during the COVID-19 response, when funds were available to improve hand washing and hygiene. Challenges include the length of time it can take to apply changes and adapt to new situations. With outbreaks, challenges are mainly around campaign coordination. Niger has a high level of vaccination activity because it suffers from different and recurrent epidemics and outbreaks (cholera, meningitis, polio, etc.), and implementation of all these campaigns requires a challenging level of coordination – especially when there are issues with vaccine interactions.

For OCV specifically, 2017 recommendations say OCV can be co-administered with other vaccines, but on the ground, questions remain around oral polio vaccine. A recent study in Bangladesh suggests that polio and cholera vaccines can be safely administered together. New SAGE recommendations will follow next year. Currently, there is confusion because online WHO recommendations say the opposite and some of the language in academic papers on this subject is confusing or discouraging. This point comes up a lot and needs to be clarified.

Discussion

- Tailoring integrations to context involves community engagement and socioanthropology, and is linked to the research agenda. Experience of what does and does not work can deconstruct preconceived ideas. More research is needed to document these behaviours and allow more and better evidence-based decisions.

- Countries may have integrated other campaigns as well, and these will also generate valuable lessons. Learning does not have to come only from OCV campaigns.
- The IFRC Campaign Support poster (see Annex 1) describes a pan-African project with three interventions, oral rehydration therapy (ORT), OCV and WASH, that looked first at enabling factors like funding, logistic capacity, timeframes, etc. Given an OCV campaign can involve hundreds of thousands of people, to a great extent these factors determine what is possible. WASH, on the other hand, is more limited in scope. This suggests that exactly where and how integration is attempted requires careful thought.
- On this point, there is need for more discussion of exactly how WASH can support OCV campaigns. There is a need to balance integration with the desired high speed of OCV campaigns, because WASH elements can take much longer. The Nepalese choice to deliver WASH messaging is a good compromise, because it is quick. But the necessary evaluations can complicate things, with the need to assess how water treatment works, whether and how containers are replaced and/or cleaned, water storage options, etc. There are many models for approaching this, with doorstep teams doing both jobs, or separate sub-teams pushing OCV and WASH. Adapting to context is essential: for example, if teams go door to door with first OCV doses, it can be confusing if they are talking about second doses at the same time as handing out tablets that are actually for water treatment.
- The correct scope for WASH interventions also requires discussion. The length of the intervention is limited if it is just distributing water treatment resources. Each campaign should look at the opportunities for WASH response offered in that particular context: for example, if communities are made aware of the need to treat water by a cholera outbreak, it may be a valuable opportunity to sell the idea of water treatment in the medium term and/or the most vulnerable times of year.
- The idea of associating prevention campaigns with long term WASH requires examination: in reality, the notion of taking 2-3 years to get long term infrastructure in place after an OCV campaign is not realistic: it does not actually happen. Moving focus to medium-term interventions that might be more effective.
- When the ICG receives OCV requests for emergency response in which countries are looking to integrate other vaccinations, that becomes a challenge for them because of funding. Integration may be the best way to deal with things at country level, and can avoid duplication of resources and services, but does require more thought on how best to aid integration planning and the budgetary components of campaigns.
- Gavi funding guidelines expect campaigns to be done in low resource areas where there are likely to be opportunities to identify children who have missed routine immunization and refer them to vaccination structures. This is a good approach to integrating a health systems-strengthening activity that has already been successful in a few places (for example, with typhoid in Nepal). Even in reactive campaigns it is possible to think in advance of other needs in the target communities. Cholera touches the entire age range and is based on a two-dose strategy, meaning that round one can be used to refine needs assessments and round two can be used to respond to those needs.
- There is a need for more discussion of integration outside the reactive/emergency context - especially for WASH. Considering that preventive campaigns will now be financed by Gavi, there should be consideration of whether – for example - WASH integration could be added to countries' operational costs. From a roadmap perspective it is important to ask countries to do WASH, but without financing it will be impossible in many contexts.
- From Gavi's point of view, WASH integration brings great benefits not only with cholera, but also for typhoid, malaria and other diseases. While Gavi is bound by its emphasis on vaccination, it is looking at ways to integrate other activities through systems-strengthening grants.
- Gavi financing for operational costs is intended to help, not replace, national effort. As with other diseases, countries and WHO will also need to look to other partners and donors for WASH interventions. National cholera control plans and MYPs will be good advocacy tools for this purpose.

- Countries are encouraged to contact Gavi with thoughts on integration – especially of different vaccination programmes – with a view to further discussion and possible development of proposals. Gavi is currently seeing a lot of budgets below the $0.65/dose ceiling, so there is still room within allocated funds to integrate other strategies – especially if those are around identifying the need for other vaccines. Equity and equalisation of coverage is very welcome and highly encouraged. There are also separate funding streams available for zero dose children that should be considered.

Country-focused workshop: MYP considerations & development

In this session countries presented their MYPs and their OCV demand projections, with a view to refining overall understanding of how much preventive vaccines countries will need and for what; and when the respective approval processes of the new Gavi framework can be expected.

Ethiopia

6,814,410 doses were approved by the GTFCC on November 3, 2021 and the OCV action plan was revised twice and submitted. Challenges include postponed delivery of the approved doses, limited cold chain capacity, inability to submit the GTFCC request as quickly as hoped, and the late release of operational costs for a reactive campaign.

Best practices have included the redirection of leftover vaccines to other campaigns at no additional operational cost; close collaboration with the national EPI (Expanded Programme on Immunization) team in the preparation and implementation of the campaigns; and planned high level national health security coordination. The NCP and hotspot analysis have already been submitted and the vaccine has been pre-approved, with the campaign planned for early 2023.

DRC

DRC's mapping of priority areas is complete, and the first draft of the NCP will be shared before the end of October 2022. A workshop will be held to validate the NCP on November 15 and 16, and the submission of the NCP to the IRP planned at the end of November. The NCP should be endorsed by government around the middle of December 2023.

For the OCV MYP, a consultant has been selected and was planned to start work the week after this meeting. 39 priority health zones have been identified (with a combined population of 12 800 424). Preventive OCV campaigns will be done in priority health zones and reactive campaigns in other zones, with flexibility built into the campaign to allow OCV campaigns to respond to evolving epidemiology. DRC is interested in piloting criteria to prioritize health zones using the tool currently being developed by the working group.

Bangladesh

Nationwide cholera surveillance is conducted through 16 sentinel surveillance sites, four with enhanced surveillance and 12 with standard surveillance. Early warning alert and surveillance (EWARS) is ongoing in Cox's Bazar. Dehydration status of diarrhoea cases at admission has been introduced into DHIS-2 and web-based disease surveillance, and a consultant will be hired for hotspot mapping based on current available data.

The OCV requirement until 2024 remains in line with the NCP (with a total of 172.9 million doses required between 2019 and 2024); but due to COVID-19 and other factors, only 5.8 million doses were received between Feb 2020 and August 2022, around 3.3% of the need projected in the NCP. However, - the NCP was drafted three years ago using estimations; when hotspot mapping is completed, the volumes of vaccine can be expected to will change. Bangladesh is working on a more accurate prediction that should be complete in Q1/Q2 2023.

Current priorities are to develop a national MYP based on hotspot mapping, and to vaccinate migrant workers and pilgrims travelling during peak cholera season.

Cameroon

NCP development in Cameroon is in the start-up phase, with the identification and prioritization of hotspots and the situational analysis completed. Definition of the coordination mechanism and its objectives will take place on 9-10 November 2022. WHO and other partners are helping with the development of the MYP. Though a formal delivery date has not been set it is hoped that this will be ready to implement in Q1 2023.

Mozambique

Hotspot mapping has been done: 35 Districts (22% of the total) contain cholera hotspots, directly affecting 10,914,967 people (35% of the population). An OCV plan has been developed based on the mapping, with a total of 30.7m doses required for full implementation. NCP development is near completion, with the only two outstanding activities, both in progress at the time of the meeting, being the capacity assessment (with a deadline of 30 October 2022) and the writing of the NCP document itself (deadline 30 November 2022). Dr Langa emphasized the need to congratulate his team for this work, who, he said, were having to use their own resources to conduct online trainings because resources are so scarce. He encouraged GTFCC members to note this reality: “We think ‘just develop an NCP,’” he said, “but a lot of work goes in, a lot of data collection. It takes time and costs money to do multisectoral engagement and it is a challenge.”

South Sudan

South Sudan confirmed a cholera outbreak after identification of an index case on 19 March 2022 in Bentiu IDP Camp, officially declaring the outbreak on 7 May. Cumulatively, there had been 389 (30 culture-confirmed) cases and one death (CFR, 0.26%) at the time of the meeting. Phased deployment of OCV is proposed, with priority given to hotspot locations in category 1 counties. Over 2.6m OCV doses were requested for these counties. 1,677,500 doses of OCV had been received in South Sudan in 2022 at the time of the meeting, and 1,584,147 doses of OCV had been administered in six counties (with 749,981 people fully vaccinated and 84,184 partially vaccinated and awaiting their second dose). An OCV implementation plan has been developed and costed and is being updated based on context, and an NCP has been developed and is awaiting validation.

Lessons to date have included the usefulness of weekly meetings to facilitate the effective work of the Multisectoral Coordinating Platform. Challenges have included access constraints (caused mainly by security issues, flooding and the effects of the rainy season), delays in OCV shipments to the country, and inadequate funding for in-country shipment. The urgent next step in South Sudan is to deploy the required OCV doses to hotspot counties as flooding and other risk factors still exist.

Bénin

Bénin had to develop a response plan for a 2021-2022 cholera epidemic, which was successfully implemented. In June 2022, Bénin completed the NCP 2022-2026 with contributions from all

stakeholders, and this was submitted to the GTFCC for review in July 2022. Bénin has never yet used OCV (neither preventive nor reactive). Cholera hotspots have been identified in 15 municipalities across seven Departments with a total population of 4,063,659. This population will be gradually covered by cholera vaccination over the next five years. Preventive OCV campaigns will be conducted in hotspots according to a predefined schedule modified according to the outcome of requests for doses to the GTFCC.

Nepal

Nepal has suffered several cholera outbreaks in the past decade. A cholera preparedness and response plan has been developed predicated on leadership and governance from a steering committee for enteric disease formed of different technical and supporting agencies; guidelines for national preparedness and response with a detailed action plan; active WASH clusters; and regular review meetings to update progress. Surveillance and reporting are key to the plan, with cholera one of the notifiable diseases in EWARS (across 118 sentinel sites), active surveillance in 21 health facilities, a network of national and provincial laboratories, and routine water surveillance. Capacity building is being provided for rapid response teams (RRT), medical personnel and in risk communication and community engagement (RCCE), with WASH training for health workers, strengthening of community detection capacity with through rapid diagnostic testing (RDT) kits. Nepal has experience of vaccination campaigns in the past and has a continued need for OCV in Kathmandu and other hotspots.

The way forward from here is to work in four key areas: food, water, behaviour and waste. Ongoing priority areas for action include sensitizing and supporting relevant agencies on ongoing cholera control; compulsory chlorination; ensuring safe drinking water supply by repairing water supply pipelines and drainage systems; sensitizing local communities about water supply chlorination, especially during the pre-monsoon and monsoon seasons; providing resources to improve surveillance (strengthening RRTs) and WASH, especially in outbreak areas; ensuring safe waste management so water sources are not contaminated; ensuring food safety through rigorous monitoring and testing; strengthening labs for food and water sample testing, and giving the highest priority to monitoring and supervision of these ongoing activities.

Niger

Hotspots have been identified and validated, using the GTFCC tool, in 21 districts across seven regions. 44% of the country's total population (9,419,410 people) will be targeted with OCV. NCP development has been challenging and had to be suspended due to contextual constraints; Efforts are underway to restart it, and OCV will feature prominently in the future plan. Niger has experience in organizing mass vaccination campaigns against cholera dating back to 2016. Projected vaccine needs for 2023 and 2026 are 10,744,720 doses and 11,982,057 doses respectively. An MYP is likely to be a useful tool as there is a high likelihood that it will not be possible to do everything in the first year of the plan.

Somalia

Somalia has projected OCV requirements for each year between 2022 and 2026, with a total need over this period of 15.5m doses for a target population of 7.6m, 1.9m of whom are IDPs – noting that these projections are subject to change based on population figures at time of implementation, the epidemiological situation, and the availability of funding. A five-year NCP was developed but has now run its course (it covered 2017-2021). Throughout its implementation it reduced the cholera caseload greatly with OCV and other interventions. Somalia is grateful for the ICG's fast turnaround times. One historical challenge in implementing OCV campaigns has the national tax on humanitarian supplies, but the government has now agreed a waiver and currently it is not a problem – though this could change.

Uganda

Uganda's 2017-2022 NCP has recently come to an end. Over the course of the plan, preventative vaccination was carried out in 11 districts, with reactive campaigns in a further three districts. No outbreaks have yet been reported in districts that had OCV. A review of the expired NCP is ongoing, and hotspot mapping is planned for November 2022, after which a new NCP will be developed, guided by a particular focus on issues of population growth and needs in districts hosting refugees. Approximately six million doses are expected to be required over the next five years.

Kenya

The launch of Kenya's NCP is planned for October 2022. A pre-emptive OCV campaign is planned in Dadaab refugee camp and surrounding host communities, with a target population of 883,634. The ICG has approved 883,634 round one doses. Hotspot analysis is complete, based on incidence, persistence and WASH indicators, and projects an overall need for 32.6m doses for preventive campaigns in 80 districts over the next three years.

Discussion

- The IRP is a team of independent experts working *pro bono* and subject to availability, which can affect timelines. For example, Bénin's plan was submitted in French, so funds needed to be found for translation. Issues like this explain why things take time – not because some requests are more or less important than others, but because the IRP is a small team organising itself and some processes are time-consuming. The steering committee is working on trying to find longer term solutions to these issues.
- Gavi advises that the most important thing in order to speed up applications is to ensure that they are as strong as possible before they go to the review committee, raising very few questions, and only ones that are easy to address.
- Looking at actual activities taking place on the ground, countries are adapting tools and moving forward with methods that others have probably never seen. The need for technical support and planning assistance on NCPs and other things is immediate. Integration planning should be happening now too, building rationales, scoping needs to address within plans, along with M&E and delivery strategies, so that things are ready to go as soon as they are approved and funded. Many countries struggle with fragmented systems and will need help.
- The GTFCC should reconsider its thresholds for declaring outbreaks in endemic countries. The current case definition confuses partners who fail to differentiate between AWD and cholera, resulting in over-reporting. (The group is already engaged in refining case definitions).
- The last past few years we've seen downgrading of demand to match size of supply, but the real demand has to be evident – even if it may seem unfair to ask countries to plan MYPs that require numbers of doses that are realistically far above what they will actually be able to get. It is important that requests articulate real needs and the rationale for them, not that they reflect current supply. To incentivise and achieve increases in supply, the market needs approved requests that reflect actual demand. Once allocation principles are complete, these will help manage the situation.
- There is an unresolved paradox in the fact that this argument was made frequently, while at the same time countries were being told "to be realistic in planning… don't plan for 30 million people."
- Countries' ability to make justifiable plans will be increased by clearer technical guidance around hotspot analysis and where and how vaccines should be used, with suggested incidence thresholds for vaccine use, acknowledging surveillance limitations, so countries can make informed decisions about where vaccine might have most impact. Mapping improvements should continue because this is what countries will use to make better-justified applications.
- Allocation needs to consider not only need, health impact, burden and equity, but also feasibility of implementation.

- In preventive campaigns, experience suggests countries can implement big numbers: Bangladesh, for example, vaccinated 2.3m people in six days with excellent coordination.
- The new Gavi application process is very stringent, so there is a need to expedite training more quickly to meet needs of short-term demand, and better orient countries to a changing and difficult process. Countries must be prepared if they are going to be asked to put in applications in 2023.
- So far, most calls for assistance have been for training and technical support – e.g., from consultants.
- Countries would benefit from greater collaboration between their cholera and EPI teams, especially given the EPI teams' broad experience working with Gavi. This would have to be approached carefully given the large amount of work already demanded from countries in terms of NCP development etc. The GTFCC must help countries clarify timeframes and how this is expected to happen, without overburdening them with competing processes. Integration has to apply to the GTFCC too!

Finalizing working group priorities for 2023

Ms Bouhenia presented a non-prioritized list of activities to consider for the 2023 workplan (Figure 8, in the understanding that the working group can address planning and feasibility later.

Figure 7: Proposed 2023 workplan for the OCV working group

Thematic area	Proposed activities for 2023
Guidance	• Selection of identified hotspots for OCV use (part of MYP) • Strengthen GTFCC process for reviewing preventive requests • Support Gavi with completion of market shaping roadmap • Guidelines for OCV allocation for preventive campaigns • Support ICG Secretariat with revision of ICG guidelines on reactive use of OCV • Papers summarizing evidence of protection from single dose use, co-administration
Operations	• Prepare training materials and conduct training of MOH and consultants for OCV • Develop online version of request/campaign training • Develop tools and guidance documents to ensure standardized campaign M&E (continued – OCRA pilots; new – review campaign evaluation and integration tools; other?) • Develop webinar to build awareness of new Gavi OCV request process; make documents available on GTFCC website • OCV strategy (NEW) • Demand documentation (Gavi – expression of interest)
Data sharing	• Develop dashboard for OCV requests, shipments and campaigns • Review OCV use 2013-2021 • Impact of COVID on OCV campaigns

She also summarized the following new areas of interest for research that emerged from earlier discussions:

- Evidence to demonstrate safe use of OCV in pregnant women (determining whether new research is needed versus existing Shanchol research)

- Duration of protection from OCV (including a possible case study on lessons from Haiti)
- Documenting the impact of CTC on OCV programmes
- Documenting vaccine effectiveness of Euvichol
- Work to bring research and application more cohesively together, strengthening feedback and updates from research partners to the working group.

At secretariat and CSP level, the GTFCC is currently running an exercise to clarify priority actions, especially given widespread resource limitations.

It will be critically important to allocate responsibility for different pieces, in frank discussion with partners and considering the real resources available. All members need to be clear and open about the time each can dedicate to this work – this is a common issue across all the GTFCC working groups and the Secretariat.

ICG announcement

The ICG members present gave a short presentation announcing and explaining the difficult but necessary decision they had taken the previous week to temporarily suspend allocation of second doses for reactive campaigns. This decision was taken because of current supply constraints and the fact that it will save lives, allowing more people to be vaccinated in outbreak responses.

The ICG acknowledges the fact that a lot of communications work will be needed now to avoid confusion. The one-dose strategy will need to be well communicated, particularly as it carries some additional risk (e.g. long outbreaks resulting in reinfection, loss of confidence in OCV, consequent vaccine hesitancy and so on). The formal two-dose recommendation is not being revised. This decision should not affect prevention plans. Countries should still do prevention planning and the market still needs demand forecasts. Acceleration of prevention programmes is more critical now than ever.

This decision will be regularly reviewed and a two-dose strategy will be resumed as soon as possible.

With Syria, Haiti, Lebanon, Malawi, Mozambique and possibly Bangladesh and Pakistan post-Monsoon, the importance of solutions for early detection of outbreaks is higher than ever.

Even more new ICG requests are in process.

This is a critical time for cholera control, and we will only get through it successfully by coordinating, collaborating and working together.

A number of participants spoke of sharing the ICG's concerns about the global OCV situation. Gavi representatives underlined their intention to continue working closely with the UNICEF Supply Division and OCV manufacturers to support countries and secure vaccines and deliver vaccines.

It was noted that evidence for a single dose strategy suggests protection is longer than six months in people older than five, up to a year or more. This also happened in Bangladesh, where campaigns had to be suspended after one dose because of COVID-19. After the pandemic, the country decided to restart vaccination from scratch because there is not enough strong evidence to do otherwise. These are the challenges of cholera: not enough data and not enough evidence.

Closing statement

***Philippe Barboza**, GTFCC*

Dr Barboza closed the meeting with thanks to everyone for their contributions and their support, and thanks to the support staff and translators who hosted the meeting. The GTFCC survives because it is a partnership.

He also thanked manufacturers for increasing production.

Special thanks and appreciation were given to Thomas Mollet, who is moving on from his post at IFRC.

Dr Barboza's final plea was for everyone to "stay with us, bear with us:" the cholera situation is serious. A battle has been lost, with cholera now flaring up everywhere, but the war is still in the balance. The cholera community will continue to make the best decisions it can to allocate the available vaccines and find and implement the best ways to provide support, clinical care, and access to health care. It is the ultimate priority, and a hard moral obligation, to do everything we can to reduce mortality.

More support is needed if success is to be possible, but it can be done.