GLOBAL TASK FORCE ON CHOLERA CONTROL

ORAL CHOLERA VACCINE USE IN COMPLEX EMERGENCIES: WHAT NEXT?

REPORT

WHO MEETING, 14–16 DECEMBER 2005
CAIRO, EGYPT

World Health Organization

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Contents

Summary

Two WHO meetings – in 1999 and 2002 – had examined the potential use of oral cholera vaccines (OCV) as an additional public health tool. In the light of the work accomplished since 2002, the Global Task Force on Cholera Control decided to convene a third meeting to re-examine with a group of experts the role that OCV might play in preventing potential cholera outbreaks in crisis situations and to discuss the use of OCV in endemic settings. The aim of the meeting was to agree a framework for WHO recommendations on these subjects and to consider the pertinence of further demonstration projects in endemic settings or of scaling up vaccination campaigns to intervention projects.

The meeting was convened by the Global Task Force on Cholera Control and hosted by the WHO Regional Office for the Eastern Mediterranean; more than 40 participants were present, representing cholera-prone countries that had already used or expressed interest in using OCV, humanitarian organizations, scientific institutions, United Nations agencies and WHO headquarters and regional and country offices. An OCV manufacturer, granted observer status, attended sessions 1 to 6 but not the two working group sessions aimed at developing recommendations on the use of OCV in complex emergencies and endemic settings.

The six sessions of the meeting addressed key issues, including currently available vaccines, crisis situations, and the cholera control measures usually recommended. Working group sessions elaborated the recommendations relating to use of OCV *(1)* in complex emergencies and *(2)* in endemic settings.

With respect to OCV use in emergency settings, the need for a multidisciplinary approach was stressed, as was the need to consider cholera and its prevention and control within the larger context of public health priorities in times of crisis.

In considering OCV use in endemic settings, all participants agreed that further data need to be collected before a clear definition of endemicity and potential vaccination strategies can be established. Results of further studies on the vaccines per se are also awaited.

Finally, a decision-making tool for assessing the pertinence of OCV use in emergency settings was drafted; it was finalized by an ad-hoc working group convened in Geneva on 1 March 2006. The document is now ready for field testing and can be found in Annex 1 of this report.

Introduction

Although well known since the nineteenth century, cholera still remains the most feared and stigmatized diarrhoeal disease. Linked to inadequate environmental health, it affects the poorest and most vulnerable populations. The burden it imposes on health care systems is enormous, as is the financial cost for its victims. Moreover, fearful of possible commercial sanctions that would prevent the export of food products, countries are often reluctant to report cases and seek support. Heavy death tolls are regularly reported when outbreaks occur, either in crisis situations, when people are displaced to overcrowded settlements, or in endemic settings, among the inhabitants of urban slums or in poor rural areas. In disaster situations, whether man-made or natural, the possibility of cholera frequently triggers panic – even when the risk of outbreak appears extremely limited.

The following is the WHO standard case definition of cholera:

- In an area where the disease is not known to be present, a patient aged five years or more develops severe dehydration or dies from acute watery diarrhoea.
- In an area where there is a cholera epidemic, a patient aged five years or more develops acute watery diarrhoea, with or without vomiting.[1]

Implementation of the prevention and control measures usually recommended, including improvement of water and sanitation, remains a challenge, both in urban slums and in crisis situations. To date, there has been no concrete global improvement, despite efforts made at country level; indeed, disease incidence has even increased in recent years. Notification of cholera is compulsory, yet cases are commonly under-reported. Predicting potential outbreaks remains difficult and is often complicated by the lack of data on trends and patterns over time.

It is clear that additional public health tools – such as vaccines – can play a critical role in the control of cholera. Pre-emptive use of oral cholera vaccines (OCV) in emergency situations was recommended by WHO in 1999, and this general recommendation remains valid *(1, 2)*. However, vaccines must be used in appropriate circumstances, where they can provide a definite benefit compared with the recommended control measures alone and will not jeopardize the response to other health priorities. Identifying the population at risk of epidemic cholera is therefore a key element in considering the use of OCV, as is the cost-effectiveness of such an intervention. Several mass vaccination campaigns have already been carried out in crisis situations, and the evidence provided by these interventions can be used as the basis for developing recommendations for appropriate use of OCV.

The WHO meeting held in Cairo on 14–16 December 2005 was intended to establish a framework for recommendations on OCV use in complex emergencies and natural disasters, as well as in endemic settings. Experience gained over the previous three years from intervention projects in complex emergencies in Darfur, Sudan, and Aceh, Indonesia, and from a demonstration project in the endemic setting of Beira, Mozambique, provided the basis for discussion of the pertinence of developing assessment tools for cholera outbreaks and for identification of opportunities for – as well as possible constraints and limitations to – OCV use for mass vaccination campaigns. While a pragmatic public health approach was adopted, the scientific bases of different vaccines were also

[1] Cholera is known to occur in children under five years of age but cannot be differentiated on clinical grounds.

reviewed and updates on recent research were reported.

The aims of the meeting were:

- to review the recent use of cholera vaccines in crisis situations;
- to develop WHO recommendations for OCV use in crisis situations, in order to make efficient and timely use of limited resources;
- to revisit the pertinence of demonstration projects in endemic settings, asking whether the evidence on feasibility and effectiveness gathered during the Beira project is sufficient for scaling up the interventions in endemic settings.

The following issues were discussed:

- Will cholera remain a public health problem in the future?
- Based on country examples, what are the main challenges to improving environmental management in crisis situations?
- Are tools for risk assessments needed?
- What role can vaccines play in cholera control in complex emergencies and natural disasters?
- What role should vaccines play in cholera control in endemic settings?
- Are new vaccines/formulations needed or are the available vaccines sufficient?
- Should a vaccine stockpile be developed and, if so, under what conditions?

1. Available vaccines and new developments

This session was intended to update all participants on the current status of available cholera vaccines, reviewing vaccines under development *(3)* and discussing the concepts of herd protection and herd amplification. It concluded with an overview of recent projects conducted in Asia by the International Vaccine Institute (IVI).

1.1 Currently available OCV, vaccines under development and formulation

Because of its low protective efficacy and the frequent occurrence of severe adverse reactions, the early parenteral cholera vaccine was never recommended for use (4). To date, two oral vaccines have been licensed internationally. One consists of killed whole-cell Vibrio cholerae O1 with purified recombinant B-subunit of cholera toxin (WC/rBS). It is administered in two doses, with an interval of 10–14 days between doses. A large volume of liquid (75–150 ml) is needed for administration, meaning that the vaccine cannot be given to children under two years of age. In addition, no data are available on use of the vaccine in younger age groups. Protection starts 10 days after ingestion of the second dose and has been shown to reach 85–90% after six months in all age groups, declining to 62% at one year among adults (5). This vaccine, currently produced in Sweden, has been granted WHO prequalification.

The second licensed vaccine consists of an attenuated, live, and genetically modified *V. cholerae* O1 strain (CVD 103-HgR) *(6)*. It is administered in a single dose to individuals aged two years and over; protection starts eight days after ingestion *(7)*. Although a 95% seroconversion and protection was observed during a challenge study, a large field trial undertaken in Indonesia, in circumstances that complicated interpretation, failed to demonstrate convincing protection *(8)*. The manufacturer stopped production in 2004 and the vaccine, although licensed, is currently unavailable.

Technology transfer to Viet Nam has generated a variant of the killed whole-cell vaccine containing no recombinant B-subunit (i.e. WC vaccine). This vaccine is currently produced and used only in Viet Nam; it is given in two doses 10–14 days apart, without the need for a buffer solution. Protective efficacy of a first-generation monovalent (anti-O1) Vietnamese cholera vaccine was shown during an outbreak in Hue to be 66% (68% in children) 8–10 months after vaccination *(9)*. Killed O139 whole cells were added to the Vietnamese vaccine following the emergence of the new form of epidemic cholera caused by this serogroup: a study found the bivalent vaccine to be safe and immunogenic in adults and children of one year and older *(10)*. A phase III clinical trial is currently being prepared in Kolkata, India, in the light of a possible transfer of technology to India.

A number of other live oral vaccines are under development in the USA (Peru 15, CVD 110, 111, 112) *(11)* and in Cuba (Cuban 638 strain) *(12)*. Results are promising and phase II and III trials are planned. In addition, research is currently being conducted, in France and in USA, on parenteral conjugate vaccines, and evaluations are planned in countries with endemic cholera.

Limitations of the currently available and internationally licensed two-dose vaccine became apparent during large-scale intervention projects conducted during the past three years: the need for buffer solution means a need for water, and administration in two doses 10–14 days apart implies the need to reach the same population twice. Thus there are important logistic constraints (clean water, cold chain, weight and volume of vaccines) and implementation difficulties in emergencies, where the population at risk is constantly moving and often situated in areas with limited access. One of the challenges faced by researchers is therefore to improve vaccine formulation to facilitate transport, storage, and administration. Ideally, a vaccine could be administered in a single dose without water

and buffer, would not require a cold chain, could be administered to children under two years of age, and would confer long-term protection. It is hoped that current research and development involving live attenuated vaccines and preparations for transcutaneous or nasal administration may lead to improvements in this regard.

The Board of the Global Alliance for Vaccines and Immunization (GAVI) has decided that half of the resources of the Vaccine Fund should be allocated to activities that support the introduction of and access to new and under-used vaccines. The selection of projects for support by GAVI should be based on invited "investment case" proposals.

1.2 Killed and live vaccines: pros and cons

Two types of OCV are currently licensed or under development – live and killed. The different specifications of the two types may mean that one or the other is preferred in a particular situation, according to the needs identified. Their cold-chain requirements, stability, mode of administration and method of action, and those of the conjugate parenteral vaccine currently under development, have been compared.

The limitations of the currently available two-dose killed vaccine in emergency settings, where logistic and practical constraints abound, have been demonstrated, but use of this vaccine in a routine context is much more easily managed. However, since efficacy requirements may be lower in an emergency context, vaccines specifically designed for emergency public health applications should be considered *(13,14)*.

1.3 Herd protection and herd amplification

In researching the public health impact of cholera immunization, the concepts of herd protection[1] and herd amplification, which arose from recent environmental studies, are important issues that merit examination. If these concepts prove sound, herd protection may have a major role in increasing the impact of vaccination and reducing the cost and burden of cholera – factors that are essential elements in any consideration of the future use of cholera vaccines.

In the 1985 cholera vaccine trial in Bangladesh, subjects were individually randomized to receive one of three agents: BS-WC vaccine, WC only, or placebo. A recent re-analysis of the data compared baris[2] where a high proportion of residents were vaccinated with baris where a lower proportion were vaccinated (range 4–65%) *(15)*. Herd protection would be demonstrated by placebo recipients in the baris with higher vaccine coverage having greater protection than placebo controls in baris with lower coverage. Herd protection might also reduce the incidence of cholera in vaccinated subjects if their neighbours were also vaccinated.

The new analysis established that there was an additional indirect protective effect among both vaccinated and non-vaccinated individuals when a high proportion of the population was vaccinated, and a possible reduction of the incidence of cholera in all age groups. The public health impact of killed OCV may thus have been underestimated in the past, as only the conventional protection

[1] When dealing with a killed vaccine, the term herd protection is preferred to herd immunity as unvaccinated persons do not develop antibodies.

[2] A bari is a unit of dwelling in rural Bangladesh, usually based on patrilineal relationship, consisting of more than one hut in the same compound.

efficacy of the vaccine was measured by individually randomized designs. Herd protection should be assessed through randomized cluster studies. A substantial positive indirect effect was evident when a high proportion of the population was vaccinated with OCV, with a possible reduction in the incidence of cholera among all age groups.

A number of factors may colour these conclusions. Statistical results may have been affected by the particular setting, i.e. the small micro-environments created by the completely separated baris: the same study conducted in urban settings, with higher densities of population and dwellings, might lead to a different transmission pattern. Efficient health education programmes and climatic factors are also likely to have an impact on the evolution of epidemics. In addition, the cycle of *V. cholerae* between its human host and the environment increases the number of pathogenic strains and may up-regulate virulence. The human intestine is therefore a crucial link and part of the ecological niche of *V cholerae*: the human system seems to be the amplifier equally of the *V. cholerae* and of the vibriophages, the role of which is still unclear but which seems to contribute to ending the epidemic episodes by infecting and lysing the bacteria *(16)*.

The design of future vaccine evaluations and efficacy studies will need to consider the role of herd protection. The hypothetical existence of significant herd protection will have implications for the choice of target population for cholera vaccination. It is likely that access to the vaccine might be enhanced for groups who do not usually have access to or seek treatment. It remains to be determined how these factors will influence the development of strategies that focus on reaching a particular threshold level of vaccination in order to achieve an acceptable level of protection in a community.

1.4 Ongoing IVI cholera vaccine projects in Asia

Within the framework of its Diseases of the Most Impoverished (DOMI) programme, IVI is currently conducting several cholera vaccine projects throughout Asia, focusing on different aspects of the disease – disease burden, OCV efficacy, economic and sociobehavioural impacts of cholera.

In Viet Nam, current studies are focusing on the duration of protection conferred by OCV. Since 1980, when cholera was first documented in the city of Hue, outbreaks have occurred about every three years. Mass vaccination campaigns were carried out in 1998 and 2000. An outbreak in 2003 was used as an opportunity to assess the potentially longer-term protection conferred by the locally produced cholera vaccine. In a case–control study of 69 cases and 276 controls, a protective efficacy of 50% was found three to five years after vaccination *(17)*. Future studies need to address the duration of protection following mass immunization, and the issue of financing schemes for sustainable vaccine supply and delivery.

In Kolkata, India, a phase III clinical trial of the Vietnamese vaccine is being prepared to support the submission of this vaccine – if produced by an Indian manufacturer – to WHO for prequalification. Only a WHO-prequalified product can achieve widespread international acceptance and use.

The Peru 15 candidate live vaccine, which is safe and immunogenic in adults *(11)*, has been tested in a double-blind, placebo-controlled, randomized study for safety and immunogenicity in children. Results are promising and suggest the need for a large phase III trial.

A series of economic and sociobehavioural studies have been undertaken to provide a clearer picture of the cost of illness for governments and affected families, as well as to quantify the perceived need for cholera vaccines among communities in south-east Asia.

2. Crisis situations and cholera control

The aim of this session was to define the concept of complex emergencies and to summarize field experience of cholera risk assessment, surveillance, and data collection, and the challenges of cholera control measures.

2.1 Complex emergencies and natural disasters: definition and challenges

Several definitions – political, humanitarian and sociocultural – describe the blurred concept of complex emergencies. The humanitarian community, through the Interagency Standing Committee (IASC), has been working on a new definition and on an integrated response to complex emergencies. A new cluster approach has been agreed upon and is currently being tested in the field by United Nations agencies and their partners. It was not the purpose of this session to attempt a comprehensive review of definitions in current use: instead, a pragmatic public health perspective was adopted, aiming principally to highlight the challenges and health priorities.

All participants agreed to define complex emergencies in the following terms:

- a large part of the population is affected, leading to potential massive movements of populations;
- coping capacities of the local and national authorities are overwhelmed by the magnitude of man-made or natural disasters;
- numerous national and international actors may participate in the relief efforts.

The first consequence of a complex emergency is the upheaval of usual life and the emergence of "new" vulnerable population groups: basic infrastructure is disrupted, and people are displaced to overcrowded and unsanitary sites. Food supplies are scarce, leading to potential malnutrition, and insecurity often prevails. All these factors have an impact on the health status of the population. People living in overcrowded camps, with poor environmental status and a lack of clean water, are exposed to a higher risk of cholera transmission if *V. cholerae* is endemic in the area or has been introduced through population movements .

Uncontrolled rumours and panic are often rife: in every catastrophe, false beliefs regarding plagues and epidemics transmitted by dead bodies tend to be widespread. In such contexts, cholera remains, rightly or wrongly, the disease most feared by the population and by the authorities.

Restoring an acceptable health status presents a number of varied challenges: health concerns are numerous and prioritizing them is crucial. The involvement of numerous actors makes coordination critical if duplication of effort or mutually interfering projects are to be avoided. Time is of the essence and urgent action is required. The decision-making and preparatory phase is often extremely short. Access to vulnerable populations is frequently limited by specific geographical difficulties, further natural disasters, a volatile security environment, or mass population movements.

2.2 Risk assessment for cholera outbreaks

The occurrence, spread, and extent of a cholera outbreak are extremely difficult to predict. They depend on a multiplicity of well-known factors, including local endemicity, living conditions, forced

or voluntary population movements, environmental and cultural factors, and the effectiveness of any control measures put in place. Even where there is the detailed knowledge that is essential for assessing the risk of cholera in a specific situation, unexpected scenarios commonly make it unrealistic to attempt to quantify that risk. In some endemic situations, where outbreaks tend to occur at regular intervals, seasonal recrudescence can be anticipated; elsewhere, the occurrence and spread of cholera remain limited and their prediction requires a thorough analysis of each situation. The establishment of an epidemiological surveillance system that will provide baseline data and trends is thus a key element in directing the potential use of OCV.

2.3 Surveillance and data gathering in complex emergencies

If the early warning system is a weak point in many countries, surveillance and data gathering in a complex emergency are even more problematic. Public health surveillance has been identified as one of the top 10 health priorities in emergencies, but the challenges are enormous. In the case of cholera, the task is complicated by the stigma attached to the disease: several countries are reluctant to report cholera cases for fear of commercial sanctions. The current International Health Regulations (IHR) designate cholera as one of the three diseases requiring WHO notification. By adopting the revised IHR in 2005, the World Health Assembly indicated a willingness to remove cholera from the list of notifiable diseases; this change should be implemented shortly and should encourage all countries to openly recognize cholera cases, leading to better national and global surveillance and thence to improved preparedness and response. The introduction of a rapid, easy-to-use and affordable diagnostic test, currently under development, will be critical.

In emergency situations, a surveillance system should be established in three phases:

1. An initial assessment should be conducted: specific surveys should be carried out and any available pre-emergency information (on endemic diseases, nutritional and immunization status, etc.) should be reviewed.

2. Surveillance should be simple and reactive, i.e. should respond to the most urgent needs generated by the emergency. The risks associated with a specific situation and the immediate public health consequences should be assessed. The WHO standardized case definition for suspected cholera cases should be disseminated to facilitate early detection of cases.

3. In the post-emergency reconstruction phase, the surveillance system set up for the emergency should be integrated into the usual surveillance system.

One of the main challenges is to establish a system that is both reactive and sustainable; this is particularly difficult when resources are scarce and security cannot be ensured. A pre-emptive approach should therefore be encouraged, with countries at risk doing everything possible to enhance preparedness plans.

2.4 Water and sanitation: challenges and cost

Because cholera is a waterborne disease, water supply and sanitation status are key issues in the prevention and management of outbreaks. The example of Darfur, Sudan, offers valuable indications of the cost, impact, and challenges of water and sanitation projects in complex emergencies and of the role of such projects in preventing cholera outbreaks.

Ideally, an integrated approach couples the provision of safe, sufficient, and equitably accessible water with adequate sanitation and health education adapted to the sociocultural background of

the community.[1] In Darfur, at the beginning of the humanitarian intervention in May 2004, only 20% of the internally displaced persons (IDPs) living in areas reachable by the United Nations agencies[2] had access to adequate water, and only about 5% to proper sanitation; by September 2005, 16 months later, these figures had risen to 52% and 76%.[3] Clearly, despite the enormous effort provided by all humanitarian bodies active in the field for more than a year, a significant number of people still lacked access to minimum water supply and sanitation facilities. This situation serves also to illustrates the obstacles faced by humanitarian workers – lack of human and financial resources, logistic constraints, limited access to IDP camps, and poor planning and coordination – all of which conspire to prevent sustained implementation and maintenance.

The exact cost of improved water and sanitation is difficult to establish; a comparison of the costs of different interventions is therefore needed. An average costing[4] made in Darfur indicated that approximately US$ 16 600 is needed annually to provide and maintain adequate water and sanitation for 1000 people. The cost–benefit of improved water and sanitation, from both health and socioeconomic perspectives, is seen mainly in the reduction of waterborne diseases, which lowers health-related costs and reduces morbidity, leading to higher productivity and better school attendance.

Achieving acceptable levels of water supply and sanitation in a crisis situation is a long-term and complex process. If assessment indicates a risk of cholera outbreaks before the environmental status can be improved and adequate water and sanitation provided, the use of OCV could be considered. While OCV obviously cannot substitute for water and sanitation projects, they could be used as an additional public health tool to provide extra short-term protection, inscribed in a sustainable perspective. The balance between different interventions depends in large part on the local context.

2.5 Response to a cholera outbreak

The usual response to cholera outbreaks is illustrated by the wide experience of Médecins Sans Frontières (MSF), whose emergency intervention teams are sent when an outbreak is detected and local response capacity is overwhelmed.

An early warning system using standard case definitions is essential to trigger the alert promptly. This is particularly critical in high-risk situations, such as in refugee camps and urban slums, and among displaced populations. The outbreak definition should take into account essential background information, including the occurrence of previous cases or outbreaks and endemicity.

- In endemic areas: doubling of cases over three consecutives weeks or increase in cases compared with the previous year.
- In non-endemic areas: increasing number of confirmed cases.
- Increasing number of adults dying from watery diarrhoea.

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1 According to the Sphere Project, which sets the Humanitarian Charter and Minimum Standards in disaster response.

2 About 1 million of the 4.5 million people displaced by the internal conflict settled in inaccessible zones.

3 These numbers are not calculated according to Sphere standards and are provided for information only; they cannot be considered as an accurate indicator of water and sanitation supplies to a population, and do not describe the actual conditions faced by the people.

4 Calculated from figures given by different partners meeting the Sphere standards in the area, including Oxfam, Care, and IRC.

The intervention strategy aims to reduce mortality[1] by ensuring access to treatment and controlling the spread of disease. To achieve this, all partners involved should be properly coordinated and those in charge of water and sanitation must be included in the response strategy. The main tools used for cholera treatment are:

- proper and timely rehydration in cholera treatment centres and oral rehydration corners;
- specific training for proper case management, including avoidance of nosocomial infections;
- sufficient pre-positioned medical supplies for case management (e.g. diarrhoeal disease kits).

To reduce the spread of disease, it is essential to improve access to water to enhance hygiene and food safety practices, to ensure effective sanitation through the use of latrines, waste management, and vector control, and to improve public information to quash rumours and disseminate correct information on cholera prevention and treatment.

The provision of safe water and sanitation in emergencies is a formidable challenge but remains the critical factor in reducing the impact of cholera outbreaks. Recommended control measures, including standardized case management, have proved effective in reducing the case-fatality rate; a comprehensive multidisciplinary approach should be adopted for dealing with a potential cholera outbreak. Although the exact cost of the different interventions is difficult to establish, they still need to be investigated and compared.

3. OCV use in crisis situations

The value and potential impact of OCV in different settings were debated on the basis of evidence accumulated since 2002. The examples of two mass vaccination campaigns – carried out in 2004 and 2005 in Darfur and Aceh – were examined and compared; the data collected should help in building a policy for use of OCV in such settings. Both campaigns took place during complex emergencies, but the nature of the emergencies and of the target populations, the simultaneous implementation of programmes to address other public health priorities, the location of the campaigns, and the partners involved were widely different.

3.1 Use of OCV in complex emergencies: recent examples

Darfur, Sudan, July 2004
In July 2004, a cholera outbreak that started in Chad was moving eastwards, towards the border with Sudan. Because OCV could be quickly made available, stakeholders present in Nyala[2] at that time, with support from the highest political level, decided to launch a mass vaccination campaign in two IDP camps on the outskirts of the city. These camps, where water supply and sanitation were poor, accommodated almost 54 800 people. The campaign was prepared and implemented in record time; within seven weeks, 87% of the 53 537 people targeted received two doses of the whole-cell killed vaccine (WC/rBS).[3]

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1 To a case-fatality rate below 2% in closed settings and urban settings or 5% in a rural environment.

2 Nyala is the capital of South Darfur state.

3 Although the 54 000 people represent only a small portion of the population at risk, the results demonstrates the feasibility of a mass vaccination campaign on a small scale.

The feasibility of a mass vaccination campaign using OCV in a small, closed setting was thus amply demonstrated, although – since no cholera case was recorded either in the vaccinated IDP camps or in surrounding unvaccinated areas – no claims for its efficacy could be made. Implementation of the campaign was enormously facilitated by the strong commitment of both national authorities and international partners, the mobilization of the IDP community, and the logistic advantages of proximity to Nyala airport. The direct costs of the campaign reached US$ 336 527, or US$ 7 per fully immunized person.

Aceh, Indonesia, March–August 2005
Following the earthquake and the tsunami that devastated several countries in south-east Asia on 26 December 2004, the Indonesian Government, perceiving a risk of a cholera outbreak, decided to implement a mass vaccination campaign in the affected areas of Aceh province and requested WHO support for this intervention. Problems of coordination, planning, and access to the affected areas, as well as significant logistic difficulties, conspired to complicate and delay the implementation, which began in March 2005. By the end of the campaign, in August 2005, 69.3% of the 78 870 people initially targeted had received two doses of whole-cell killed vaccine (WC/rBS). The direct costs of the campaign reached US$ 958 649, or US$ 18 per fully immunized person. Evidence from this campaign points clearly to the limitations[1] of using a two-dose vaccine in the context of a natural disaster *(18)*.

3.2 Cholera in complex emergencies: the added value of OCV

Evidence from Darfur indicates that a small-scale mass vaccination campaign with OCV is feasible provided that there is strong political commitment, easy access to the target population, widespread community mobilization, and involvement of all partners. The feasibility of large-scale interventions, however, is questionable: future campaigns will require solutions to the many difficulties encountered during recent mass vaccination campaigns. Suitable methodology is needed to guide the decision-making process of governments wishing to consider OCV use. The main lessons learnt from Aceh and Darfur are:

- An OCV campaign is feasible in natural and man-made disasters, provided that political commitment and good social mobilization can be achieved, good logistics can be ensured, and sufficient funds are available.
- A mass OCV vaccination campaign serves to highlight important deficiencies in water and sanitation coverage and to build the commitment of stakeholders and implementing agencies.
- OCV is only one part of a set of comprehensive public health preventive interventions.

The use of OCV thus needs to be positioned within the larger context of other public health priorities. It should be additional to health education and improvements in water and sanitation, not the sole intervention. In settings where a population is inaccessible for extended periods (for example, in detention facilities) or when the water and sanitation status cannot be rapidly improved, OCV use may be a definite benefit. The use of two-dose OCV is easier in closed settings (refugee and IDP camps, detention facilities, etc.), where population movements are limited and can be better controlled, than in open settings such as the spontaneous IPD settlements found in Aceh. The feasibility of scaling up interventions remains to be proved, and the cost–benefit should be further analysed. For the time being, the two-dose vaccine, and the logistics associated with its use, remains expensive – and cost-effectiveness is a key issue.

[1] See section 4.2.

Experience shows that, once a cholera outbreak has begun, a reactive vaccination campaign with a two-dose vaccine is almost impossible; a single dose-vaccine requiring no buffer and no cold chain, easy to administer, and providing long-term protection would provide the ideal solution. Nevertheless, efforts should be made to find ways of overcoming the limitations of the currently available vaccine. It should be stressed, however, that OCV should never be seen as a substitute for preparedness for cholera outbreaks – pre-positioning of supplies for case management, health education, and improvements in water supply and sanitation.

4. Challenges for OCV use in crisis situations

Experience in both Darfur and Aceh clearly underlines the shortcomings of a two-dose vaccine in a crisis situation. Understanding the various difficulties encountered during these two campaigns should help in finding suitable solutions to facilitate future campaigns.

4.1 Logistics: the case of Aceh

Use of the two-dose OCV in emergency settings can be seriously challenged by the onerous logistics involved. Several of the vaccine's characteristics are less than ideal for emergency settings, including its shelf-life, required storage conditions (cold chain, at between +2 °C and +8 °C), and volume (25 times greater than measles vaccine); moreover, its mode of administration demands the availability of significant volumes of clean water and requires the target population to be reached twice within a short time (10–14 days).

In Aceh, planning of the intervention was hindered by numerous factors – the weather conditions, the aftershocks that caused further damage to infrastructures, new emergencies, security deterioration, lack of telecommunication with field teams,[1] and, above all, continuous population movements, which made identification and full immunization of the target population extremely difficult *(18)*.

The overall vaccine wastage in Aceh reached 11.7%. In the first phase of the campaign, the lack of cold chain facilities at local level produced a 28% wastage rate. The vaccine's short shelf-life was also an issue: implementation of the final phase of the campaign had to be rushed in order to avoid loss of the stock. The overall logistic cost was enormous: cold chain facilities had to be rented, aeroplanes and helicopters had to be chartered, numerous human resources had to be mobilized – and the whole operation had to be repeated for administration of the second dose. The campaign had a dedicated logistic team whose work was critical to overcoming these difficulties.

Although logistic constraints can often be overcome, they usually lead to delays in implementation and significant cost increases. In each situation, the cost–benefit must be thoroughly assessed and the whole campaign planned in detail.

4.2 Challenges for mass vaccination campaigns

Experience in planning and implementing mass OCV vaccination campaigns in various settings since 1999 has helped to identify the following 12 principal challenges:

1 Because of the ongoing internal conflict, the radio system in the whole Aceh area was dismantled by the Government.

1. During natural disasters or other complex emergencies, basic infrastructures are damaged and disrupted, the population is vulnerable and subject to continual threats, and health care personnel are scarce.

2. Access to target populations is often limited by geographical factors, destruction of roads, climatic conditions, potential aftershocks, and a volatile security situation.

3. To deal with perceived but unconfirmed risks that may not be based on solid evidence, a risk assessment should be carried out: available epidemiological data, living conditions faced by the population, climatic conditions, environmental management, and cultural behaviours are key elements to be examined.

4. The target population may be difficult to identify with precision when there are continual population movements.

5. Thorough planning and preparation are crucial: coordination with partners is important, as are the assignment of responsibilities and good logistic arrangements. Functioning communications, training of field staff, adequate health education, and social mobilization programmes are other elements to be taken into account.

6. During the implementation phase, monitoring of the operations, ensuring timely delivery of supplies, and maintaining communication with community leaders are crucial.

7. Logistics must be thoroughly planned and closely monitored throughout the campaign, with the principal focus on transport and storage of supplies, transport of field teams, cold chain facilities, waste management, and reliable telecommunications.

8. An efficient surveillance system is vital for the early detection of any cholera cases that occur after the vaccination and for the implementation of specific control measures.

9. Sustained improvement in environmental management, access to safe water and proper sanitation, as well as adequate hygiene and food safety, are essential components of a comprehensive control strategy for cholera.

10. Health education constitutes a long-term effort and needs to address the vaccine itself, the vaccination campaign, and food hygiene, as well as water and environmental safety. Community involvement is critical to ensure effective social mobilization for the campaign and to avoid culturally inappropriate activities.

11. Problems with vaccine availability, affordability, and packaging (if not adequately designed) can prevent smooth implementation. Before the campaign begins, ad hoc solutions must be found .

12. The reality of a vaccination campaign inevitably differs from what was originally planned and expected. A detailed timeline helps to anticipate potential hindrances and plan alternative solutions.

Clearly, a mass vaccination campaign cannot be improvised at the last moment – it needs careful advance preparation. If time constraints do not allow for proper planning, for instance if an outbreak is about to start or has already started, OCV use may not be appropriate.

4.3 Pakistan: interagency approach and challenges for cholera control

The devastating earthquake that struck Pakistani-administered Kashmir on 8 October 2005 killed tens of thousands of people instantly and profoundly affected many more. Health infrastructures were severely damaged and numerous health priorities emerged. In the cluster approach implemented by IASC, WHO took the lead in health coordination. A surveillance system was set up as quickly as possible to ensure the early detection of and response to disease outbreaks among the affected population.

Although cholera is known to be endemic in certain areas of Pakistan, the risk of an outbreak in a high-altitude area as winter was approaching did not appear to be the main threat. Nonetheless, the early warning system identified cases of acute watery diarrhoea in early November in an IDP camp at Muzzafarabad; within two weeks, 760 cases were reported, but no deaths. Good coordination among humanitarian agencies resulted in an immediate response to the problem: sick people were treated, and water supplies, sanitation, and preventive health measures were instituted. This response, in conjunction with changing climatic conditions and the fact that the outbreak was limited to easily accessible areas inside Muzzafarabad, helped in containing the spread of the disease. The fear that cholera might reappear the following spring as the weather warmed made it imperative to start work immediately on a plan of action for preparedness and response. This raised the question of pre-emptive use of OCV and underlined the difficulties of logistic planning for this particular geographical setting.

4.4 Developing recommendations for OCV use in complex emergencies

In the light of their discussions, and to follow up on WHO meetings held in 1999 and 2002, all meeting participants agreed on the need to develop a methodology to guide the process of decision-making by governments wishing to consider vaccine use. Three groups worked to produce recommendations for the use of OCV in complex emergencies, as well as to define standardized tools for risk and feasibility assessments. Consensus was reached on the indicators to be used, although quantitative mathematical models were not widely accepted for determining risk assessment criteria given that they could be applied only to somewhat subjective determinants. Draft recommendations were discussed (see section 7), and all participants concurred with the creation of a small group that would develop a draft decision-making tool to be tested in the field.

A three-step process is recommended for the decision-making tool:

- a risk assessment for a cholera outbreak, which should be undertaken first;
- an assessment of whether key public health priorities are or can be implemented in a timely manner, combined with an analysis of the capacity to contain a possible outbreak;
- an assessment of the feasibility of an immunization campaign.

5. OCV use in endemic settings

The demonstration project carried out in Beira, Mozambique, showed that a mass vaccination campaign using OCV was feasible, acceptable, and effective for at least six months. Possible vaccination strategies and the associated challenges – as well as a model of cost-effectiveness of OCV use in endemic settings – were presented *(19)*. However, experience in different countries suggests that the concept of endemicity of cholera needs to be further defined.

5.1 Definition of endemicity: country experience

The country experiences described below highlight variations in the definitions of endemicity. Differences in the methodology used in the projects and in the attitude of national authorities towards cholera can result in different approaches to the disease – including the prevention measures to be adopted and the potential use of OCV. It is therefore important to find a definition of cholera endemicity that can be widely adopted.

West Bengal, India

Cholera is known to be endemic in West Bengal: in 2004, some two million cases of diarrhoea were reported,[1] of which more than 20% were due to cholera.[2] The dominant serotype was O1, but O139 was also present. Outbreaks are frequent and surveillance data show that the epidemic peaks occur during the monsoon, between August and October. Moreover, six of the seven known cholera pandemics originated from this region.

Efforts to achieve the long-term goals of prevention and control, through measures such as safe water supplies, adequate sanitation and environmental hygiene, and health education, have proved expensive, time-consuming, and unsustainable, and have so far had little real impact. In such a context, the use of OCV could be a short-term, convenient, and cost-effective prevention measure. A transfer of technology to an Indian manufacturer – currently under way – could make the vaccine available at an acceptable price, below US$ 1.00 per dose. To have significant public health impact in West Bengal, the vaccine should be designed for administration to children under two years of age and be effective against both O1 and O139 serotypes. The cost of mass vaccination of all Bengalis appears unrealistic, but it should be possible to target only high-risk subgroups, such as slum populations who number about 10 million (40% of the urban population). These are the poorest members of society – and the people for whom the financial burden of seeking treatment for cholera is the highest: each episode of cholera is estimated to cost US$ 5.00.

Pakistan

The absence of reported data and the limitations of the surveillance system mean that the burden of cholera in Pakistan remains unknown. Without good baseline data, it is difficult to advocate the use of OCV. However, data from the Aga Khan University in Karachi, which supports an extensive laboratory network throughout the country, has shown that endemic cholera in several parts of Pakistan affects mainly young children. Studies conducted in two urban squatter settlements in Karachi revealed an endemicity rate of about 1/1000 per year; 28% of the cases occur in children under five years of age. Seasonal peaks occur during the monsoon, from June to August.

More information is needed on a national level to provide a better definition of endemicity in Pakistan and to assess the potential for OCV use. National awareness of cholera should certainly be raised.

These two country examples show the importance of a proper definition both of cholera cases and of endemicity. A threshold of 1 case per 1000 people has been proposed, but has yet to be universally accepted. Epidemiological data still need to be collected: lack of these data is an obstacle for advocating the use of OCV. On the other hand, increasing treatment costs and rising

[1] With 1770 deaths.

[2] Infectious Diseases Hospital, Kolkata, 2004: 23.5% of the patients suffering from diarrhoeal pathogens were infected by V. cholerae (70% O1, 30% O139).

antimicrobial resistance make development of a vaccination strategy for endemic settings highly desirable, provided that the vaccine can be formulated for administration to children under two years of age and can protect against both O1 and O139 serotypes.

5.2 First demonstration project using OCV – Beira, Mozambique

Cholera is endemic in Mozambique; Maputo and Beira are the worst-affected cities. Major epidemics have been documented since the mid-1990s, and the burden of disease remains high despite control strategies. The Government of Mozambique therefore undertook a demonstration project, using OCV in an endemic setting; the aim was to acquire evidence on OCV use to complement traditionally recommended control measures *(20)*. The objective was two-fold:

- to assess the feasibility, acceptability, and coverage of a mass cholera vaccination campaign in an urban African setting with seasonal cholera outbreaks, and
- to assess the effectiveness of vaccine intervention through a case–control study.

The target population was all residents of the Esturro neighbourhood of Beira, over two years of age and not pregnant. The two rounds of vaccination with whole-cell killed vaccine (WC/rBS) took place in December 2003 and January 2004, and 57% of the target population received two doses. In the case–control study conducted in 2004 and involving 43 patients with cholera, a protective efficacy of 78% was demonstrated. The area chosen for the demonstration project has a high prevalence of human immunodeficiency virus (HIV) infection, but the project was not designed to examine the ability of OCV to protect HIV-positive individuals from cholera.

This mass vaccination project demonstrated both feasibility *(21)* and effectiveness *(22)* but left a number of important questions unanswered, including duration of the protection, existence of herd protection, protection within the HIV-positive population, and cost-effectiveness. Further studies are needed, but the project has raised expectation among the population that political authorities may soon decide to scale up cholera vaccination.

5.3 Vaccination strategies: EPI and other options

Countries interested in using OCV in endemic settings will need to design vaccination strategies that will achieve the best possible coverage. Different strategies can be envisaged:

- Integration of OCV into the Expanded Programme on Immunization (EPI). This might be complicated by the fact that the target population, the mode of vaccine administration, and the vaccination schedule differ from those involved in the current EPI, which targets mainly children.
- Specific mass vaccination campaigns could be organized but would require major financial investment given the duration of protection provided by the currently available vaccine and the need to repeat immunization periodically.
- OCV could be incorporated into the supplementary immunization activities of EPI if an immunization schedule could be defined and a sustainable funding mechanism found. GAVI could be approached to support introduction of the vaccine.

Any vaccination strategy should be based on risk mapping and should take account of high-risk groups (particular age groups and vulnerable populations living in specific geographical areas)

and feasibility. The sustainability of vaccination strategies is the paramount consideration: mass vaccination campaigns that are not sustainable may be useless – and possibly counter-productive.

5.4 Cost effectiveness in endemic settings

To demonstrate the cost-effectiveness of OCV use in endemic settings, models have been developed to determine the key variables, the most important of which appear to be the incidence of cholera and the cost of the vaccine (including delivery cost). Vaccine efficacy seems to be less important. Vaccines should thus be inexpensive and easy to administer and should be provided to inhabitants of high-risk areas.

The cost per death averted and per hospitalization averted declines with increasing cholera incidence: even a very inexpensive vaccine becomes cost-effective only when incidence exceeds 1/1000. By comparison, the same model estimates that case management, if provided through routine hospital or treatment centre care, costs about US$ 350 per death averted. Even moderately inexpensive vaccines therefore quickly become too expensive. For example, a vaccine requiring two doses at US$ 3.00 per dose will cost more than US$ 3000 per death averted, even where incidence is high. By contrast, a vaccine priced at US$ 0.40 will cost less than US$ 400 per death averted, which compares favourably with case management, especially as hospital and treatment costs will decrease.

Cholera vaccine can therefore be useful as an additional public health tool, provided that:

- it is inexpensive (including transport and delivery costs) and easy to administer;
- immunization strategies target particular age groups and are sustained in high-risk areas.

Vaccines will be cost-effective only in areas that have high rates of cholera; vaccines will not replace treatment facilities. Furthermore, a vaccine marketed over the counter may be economic for health ministries since it would shift the vaccine costs to the consumer rather than to the government.

5.5 Development of recommendations for OCV use in endemic settings

The working groups dealt with the following issues:

- recommendations on the use of OCV in endemic settings based on the experience acquired in previous demonstration projects;
- evaluation of the pertinence of further demonstration projects, and specific questions arising from previous experience;
- the need to identify potential intervention projects and develop criteria for selection of sites.

All groups agreed on the need for data and on the numerous issues to be addressed, which include the efficacy of OCV in populations with a high proportion of HIV-positive individuals, a definition of endemicity, and the cost-effectiveness of the vaccine. Work should also be done on vaccination strategies. Although use of OCV in endemic settings can be supported in principle, detailed recommendations remain to be worked out. All participants agreed to recommend the synergistic use of control measures other than vaccine, namely improvement of water supply and sanitation and health education. Demonstration projects should yield additional useful data.

6. Pertinence of a cholera vaccine stockpile

The pertinence of creating a vaccine stockpile, mentioned in the 1999 WHO recommendations, needed to be examined in the light of the work accomplished since then. The mechanism involved in maintaining existing stockpiles was described, and the only OCV manufacturer present at the meeting gave an outline of current production capacities and prices. Finally, IVI proposed a model for a potential OCV stockpile.

6.1 Existing vaccine stockpiles and ICGM mechanism

To illustrate the working mechanisms of a stockpile, the example of meningitis was presented. In the past 10 years, 700 000 cases of meningitis have been detected in Africa, with 10–50% case-fatality rates and 10–20% of survivors suffering permanent brain damage. Case management strategies rely on standardized treatment with a single dose of antibiotic; mass vaccination is the usual preventive measure for limiting epidemics. The International Coordinating Group on Meningitis (ICGM) for supply of antimeningococcal vaccine was created in 1997 with the aims of ensuring both an emergency vaccine stock and optimal use of vaccines and drugs, and of establishing a mechanism to minimize the risk of a shortage of supplies. The stockpile consists of a revolving stock, kept by the manufacturer. An appeal for funds financed the initial stock and ICGM advances the vaccines against later reimbursement.

A prepaid "immortal stock" was kept until 2003, when three million doses remained unused. Once the wastage and associated financial burden became apparent, the agreement was revised. Since then, a reserve stock has been kept by the manufacturer until a purchase order is issued by ICG. In June of each year, the unused stock is returned to the manufacturer. Countries willing to use the vaccines must submit a request, backed by epidemiological and laboratory data, with an implementation plan: ICG must respond to the request within 48 hours. However, even this revised system has shortcomings. Countries variously view ICGM as an obstacle to the acquisition of vaccines, as a low-cost retailer, or as an inspector. Political pressures are brought to bear when resources are scarce. Stock management is extremely complicated and the wastage rate is high. The reimbursement system is not perfect, resulting in erosion of the budget.

Stockpile management is difficult and expensive; the advantages and disadvantages of creating a stockpile must therefore be examined in detail and adequate stock rotation must be ensured.

6.2 Availability and cost of the current OCV

The only OCV currently available on the international market is manufactured by the Swedish Bacteriological Laboratory (SBL) – a small private company specializing in vaccine production – under the commercial name Dukoral®. Dukoral® is licensed in about 45 countries and distributed through regional partners. To date, more than 6 000 000 doses have been supplied, yet the vaccine is not widely used; production costs remain high and are not covered by the price of the vaccine – up to €5 (US$ 6.10) a dose. If large orders were placed, the price could be reduced.

Maintained in a cold chain, Dukoral® has a shelf-life of three years; according to the manufacturer, it can be kept at 25 °C for three months and at 37 °C for one month, but these storage conditions were not recognized in the prequalification process.

Currently, 200 000 doses with a shelf-life of less than 24 months could be made available within six weeks, and 500 000 doses with a shelf-life of more than 24 months within six months. Production capacities should be expanded in 2007 but, without a firm order, the two millions of doses necessary for a stockpile cannot be produced at a lower price. To facilitate logistics and reduce packaging costs, it would be possible to produce a multidose sachet.

6.3 A cholera vaccine stockpile?

The WHO recommendations of 1999 proposed the establishment of a two-million dose stockpile of cholera vaccine for use in endemic and emergency settings. However, because of the lack of precise guidelines for OCV use, the high costs involved, and the limitations that became apparent during mass vaccination projects carried out between 2000 and 2005, the stockpile was never implemented. Moreover, the only current OCV manufacturer has clearly stated that, without firm orders, its limited production capacities will not be expanded. Thus, until recommendations and guidelines are issued and promoted, the issue of a stockpile is not relevant. The subject will be raised with partners and donors after the field validation of the recommendations – and, in particular, of the decision-making tool – and when countries concerned express their willingness to implement large-scale mass vaccinations or to introduce OCV into their routine EPI.

7. Recommendations

7.1 Proposed recommendations for the use of OCV in complex emergency settings

Relevance and multidisciplinary approach:

- The relevance of oral cholera vaccination should be examined in the light of other public health priorities. Among the top 10 priorities in emergencies is the control of communicable diseases, which should always include a risk assessment for cholera.
- If a cholera vaccination campaign is deemed necessary after assessment of epidemic risk and public health priorities, water and sanitation programmes should be implemented before or concurrently with the vaccination campaign. Surveillance systems should be reinforced.
- A high level commitment by all stakeholders and national authorities is critical.

Exclusion criteria for OCV use:

- Vaccination with the current internationally available prequalified vaccine is not recommended once a cholera outbreak has started.
- An OCV campaign that would interfere with other critical public health interventions should not be carried out.
- Other exclusion criteria include: very high mortality from a range of causes; basic needs (food, shelter) not covered; an ongoing outbreak of another disease; an untenable security situation.

Development of a decision-making tool for OCV use:

- A decision-making tool[1] will help in determining the relevance of cholera vaccination in a given setting. A three-step process is proposed:
  - a risk assessment for a cholera outbreak, which should be undertaken first;
  - an assessment of whether key public health priorities are or can be implemented in a timely manner together with an analysis of the capacity to respond to a possible outbreak;
  - an assessment of the feasibility of an immunization campaign.
- The decision-making tool needs to be tested and validated in complex emergency settings.

7.2 Proposed recommendations for the use of OCV in endemic settings

Despite the limitations of the currently available vaccine identified in the public health context, the use of OCV in certain endemic situations[2] should be recommended and guidelines should be developed. Such use must be complementary to existing strategies for cholera control, such as safe water and sanitation, case management, and health education of the community.

Without jeopardizing the issue of recommendations, a number of topics still need to be addressed. Recommendations can be modified accordingly, at a later stage:

Vaccines per se:

- New vaccines with improved "fieldability"[3] and cost-effectiveness are needed. Their efficacy should be established in the field.
- Where the O139 serotype is responsible for a significant proportion of cholera cases, O139 should be included in the OCV.
- Documentation of OCV efficacy is needed in children and in HIV-positive individuals.

Surveillance, endemicity and seasonality:

- Criteria for a definition of endemicity should be established.
- Studies should be conducted to determine the best timing for vaccination (seasonality, baseline data, etc.) in order to enhance the protection of the population. Past experience has shown that a two-dose vaccine cannot be used once an outbreak has started.
- Vaccination campaigns should be accompanied by surveillance to define the population at risk and to monitor the impact of vaccination programmes (e.g. among particular age groups and spatial clusters).

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1 See Annex 1.

2 A definition of endemicity of: one or more cholera cases/1000 population at risk per year has been proposed, but no consensus was reached.

3 To be understood as the practicability of the vaccine when used in difficult field conditions.

Vaccination strategies:

- Vaccination strategies should aim for the highest possible vaccination coverage to realize the benefits of herd protection; strategies should be examined and defined according to each specific situation. Characteristics of the currently available OCV (age group, formulation, etc.) make it difficult to include the vaccine in routine EPI.
- The cost-effectiveness, sustainability, and economic viability of vaccination strategies should be assessed at country level.

Additional recommendations for WHO:

- Develop a decision-making tool and guidelines for use of OCV *(1)* in complex emergencies and *(2)* in endemic settings. An ad-hoc working group will be established to develop the draft risk assessment and decision-making tool further; the first draft was to be available for circulation among the meeting participants by the end of February 2006. After revision, the document would be submitted to partners, including meeting participants, and countries.
- Test and validate the draft decision-making tool in field conditions, at community level.
- Identify possible sites for implementation projects, as a follow-up to the demonstration projects already carried out between 2002 and 2005.
- Ensure regular meetings for review and guidance.
- Develop an information and advocacy strategy for regional offices, country offices, countries and potential donors.
- Identify funding sources.

References

1. *Potential use of oral cholera vaccines in emergency situations. Report of a meeting, Geneva, 12–13 May 1999.* Geneva, World Health Organization, 1999 (CDS/CSR/EDC/99.4).
2. *Cholera vaccines: a new public health tool? Report of a meeting, Geneva, 10–11 December 2002.* Geneva, World Health Organization, 2004 (CDS/CPE/ZFK/2004.5).
3. Girard MP et al. A review of vaccine research and development: human enteric infections. *Vaccine,* 2006, 24(15):2732–2750.
4. Cholera vaccines, a WHO position paper. *Weekly Epidemiological Record,* 2001, 76(16):117–124.
5. Jertborn M, Svennerholm AM, Holmgren J. Evaluation of different immunization schedules for oral cholera B subunit-whole cell vaccine in Swedish volunteers. *Vaccine,* 1993, 11:1007–1012.
6. Viret JF, Dietrich G, Favre D. Biosafety aspects of recombinant live oral Vibrio cholerae vaccine strain CVD 103-HgR. *Vaccine,* 2004, 22:2457–2469.
7. Tacket CO et al. Onset and duration of protective immunity in challenged volunteers after vaccination with live oral cholera vaccine CVD 103-HgR. *Journal of Infectious Diseases,* 1992, 166(4):837–841.
8. Richies E et al. Efficacy trial of single-dose live oral cholera vaccine CVD 103-HgR in North Jakarta, Indonesia, a cholera-endemic area. *Vaccine*, 2000, 18:2399–2410.
9. Trach DD et al. Field trial of a locally produced, killed, oral cholera vaccine in Vietnam. *Lancet,* 1997, 349:231–235.
10. Trach DD et al. Investigations into the safety and immunogenicity of a killed oral cholera vaccine developed in Viet Nam. *Bulletin of the World Health Organization,* 2002, 80(1):2–8.
11. Qadri F et al. Randomized controlled study of the safety and immunogenicity of Peru-15, a live attenuated oral vaccine candidate for Vibrio cholerae O1 in adult volunteers in Bangladesh. *Journal of Infectious Diseases,* 2005, 192(4):573–579.
12. Garcia L et al. The vaccine candidate Vibrio cholerae 638 is protective against cholera in healthy volunteers. *Infection and Immunity,* 2005, 73:3018–3024.
13. Calain P et al. Can oral cholera vaccination play a role in controlling a cholera outbreak? *Vaccine,* 2004, 22:2444–2451.
14. Glass RI, Steele AD. The value of cholera vaccines reassessed. *Lancet,* 2005, 366:7–9.
15. Ali M et al. Herd immunity conferred by killed oral cholera vaccines in Bangladesh: a re-analysis. *Lancet,* 2005, 366:44–49.
16. Faruque SM et al. Genetic diversity and virulence potential of environmental Vibrio cholerae population in a cholera endemic area. *Proceedings of the National Academy of Science of the United States of America,* Feb. 2004, 17;101 (7): 2123-8
17. Vu DT et al. Long-term effectiveness against cholera of oral killed whole-cell vaccine produced in Vietnam. *Vaccine,* 2006 (in press).
18. *Use of the two-dose oral cholera vaccine in the context of a major natural disaster. Report of a mass vaccination campaign in Aceh, Indonesia,* 2005. Geneva, World Health Organization, 2006 (CDS/NTD/IDM/2006.1)
19. Sack D. When should cholera vaccine be used in cholera-endemic areas? *Journal of Health and Population Nutrition,* 2003, 21:299–303.
20. *Mozambique mass campaign tests the theory.* Geneva, World Health Organization, Press Release 3, 14 January 2004.
21. Cavailler P et al. Feasibility of a mass vaccination campaign using a two-dose oral cholera in an urban cholera-endemic setting in Mozambique. *Vaccine,* 2006 24(5):4890-5.
22. Lucas M et al. Effectiveness of mass oral cholera vaccination in Beira, Mozambique. *New England Journal of Medicine,* 2005, 352:757–767.

Additional reading

Cholera, 2003. *Weekly Epidemiological Record,* 2004, 79(31):281–288.

Cholera, 2004. *Weekly Epidemiological Record,* 2005, 80(31):261–268.

Drazen JM, Klempner MS. Disaster, water, cholera, vaccines and hope. *New England Journal of Medicine,* 2005, 352(8):757–767.

Joint WHO/UNICEF statement on the use of oral cholera vaccines in tsunami-affected areas. Geneva, World Health Organization, 2005.

Sack DA, Bradley Sack R, Balakrish Nair G, Siddique AK. Cholera. *Lancet*, 2004, 363:223-233

Annex 1

Decision-making tool for the use of oral cholera vaccines in complex emergencies

Introduction

The aim of the decision-making tool described in this annex is to help determine the relevance of OCV use for mass immunization campaigns in the context of complex emergencies. For this purpose, complex emergencies are defined as situations in which:

- a large part of the population is affected, leading to potential massive population movements;
- the coping capacities of local and national authorities are overwhelmed by the magnitude of the man-made or natural disaster;
- numerous national and international actors may participate in the relief effort.

While this tool can be used in other crisis situations, WHO plans another document – to be published shortly – on the use of OCV in endemic settings.

The decision-making process follows a three-step approach (see Figure A1.1), with the relevance of OCV use being examined at each step:

- a risk assessment for a cholera outbreak, which should be undertaken first;
- an assessment of whether key public health priorities are or can be implemented in a timely manner, combined with an analysis of the capacity to contain a possible outbreak;
- an assessment of the feasibility of an immunization campaign using OCV.

Relevance of OCV use:

During the course of a complex emergency, the following public health aspects should be taken into account when examining the relevance of the potential use of OCV:

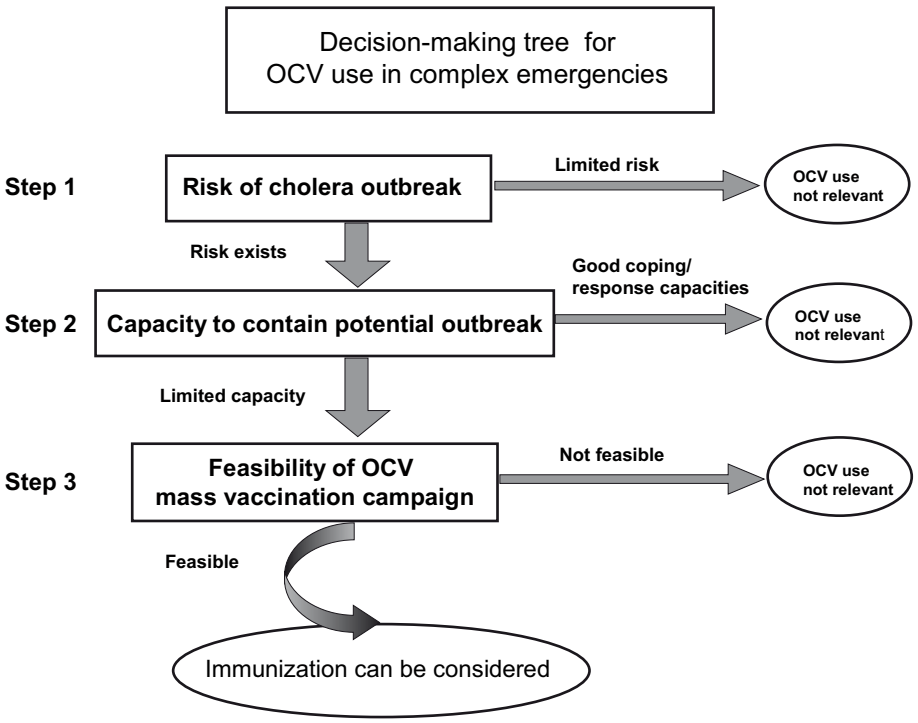
- The top 10 public health priorities in emergencies[1] include the control of communicable diseases: a risk assessment for cholera should always be part of the initial assessment.
- Regardless of whether or not OCV is used, access to sufficient safe water and adequate sanitation should be ensured.
- Priority should be given to other health priorities when:
  - mortality is very high (above the emergency threshold of 1/10 000 per day);
  - basic needs (food, shelter, basic health services, and security) are not met;.
  - an outbreak of another disease is ongoing.

[1] See WHO/HAC : http://www.who.int/mediacentre/factsheets/fs090/en/ for details.

- With the currently available internationally prequalified vaccine,[1] vaccination is not recommended in an area where an outbreak has already started.

The relevance of oral cholera vaccination should therefore be examined in the light of all public health priorities identified.

Figure A1.1 Decision-making tree



[1] Whole-cell killed V. cholerae O1 with purified recombinant B-subunit of cholera toxin (WC/rBS), administered in two doses, 10–14 days apart, in 150 ml of water mixed with a buffer.

1. Assessment of the risk of cholera outbreak

Criteria	Factors to consider	For example
Epidemiology	1. Endemicity	1. Natural immunity, e.g. have there been any cases detected within the previous five years?
	2. Risk of introduction	2. Displacement, population movements from an endemic area.
	3. Seasonality	3. Beginning/end of peak season.
Water supply	1. access to sufficient quantity of safe water	1. According to Sphere standards,[1] number of litres/person per day, quantity and quality of the water.
	2. Capacity and timing to reach and maintain standards	2. Chlorination, water trucks, water pipes, wells, etc. Risk of water supply becoming contaminated with *V. cholerae*. Poor disinfection practices, poor water handling practices. Low likelihood of protecting water supplies and reaching high level of disinfection before outbreak.
Sanitation	1. Current access and use	1. According to Sphere standards, number of persons/latrine, waste management, etc.
	2. Capacity and timing to reach and maintain standards	2. Latrines "turnover", space to build new latrines.
Hygiene	1. Levels of personal and food hygiene	1. Lack of adequate quantities of water for washing. Availability of soap for hand-washing. Poor food hygiene practices.
Population/demography	1. Density	1. Square metres per person according to Sphere standards. Number of people per household, and average household size.
	2. Vulnerability	2. Disrupted living conditions, specific vulnerable groups, long period of flight from conflict, leading to stress and malnutrition.
	3. Closed/open settings	3. Closed settings such as detention centres or refugee camps, with control of population movements.
Community	1. Sociocultural behaviours	1. Level of education, hygiene practice, funeral practices, seasonal social and religious gatherings.

[1] See http://www.sphereproject.org/handbook/index.htm.

2. Assessment of the capacity to contain a potential outbreak

Components of response	Factors to consider	For example
Magnitude of the outbreak	1. Size of affected area	Towns, open areas.
	2. Closed/open setting	Refugee camps, detention centres.
Roads, communication routes	Potential for spread of outbreak along communication routes	1. Large outbreak affecting several locations. 2. Closed refugee setting.
Health care	1. Infrastructure	1. Permanent, temporary, possibility to set up cholera treatment centres (CTC) and oral rehydration units (ORU), separate ward in the hospital.
	2. Human resources	2. Health care staff, support staff, cleaners, cooks.
	3. Accessibility	3. 24 hours/day or not, distance, remoteness.
	4. Supplies	4. Oral rehydration solution, infusion, Ringer's lactate, cholera cots, cleaning material, buckets, soap.
Health education	1. Human resources and social network	1. NGOs, schools, associations, religious leaders, persons able to transmit the right message.
	2. Accessibility	2. Possibility to reach the population, transport, cultural acceptance.
	3. Supplies	3. Banners, leaflets, loudspeakers, etc.
Water and sanitation	Capacity to provide/ improve/reinforce as needed in terms of quantity and quality	Capacity to adequately disinfect drinking-water supplies, to reach minimal coverage with sanitary facilities, and to provide adequate water and soap for personal hygiene before outbreak.
	1. Human resources	1. Trained technical personnel, able to set up and maintain systems.
	2. Supplies	2. Ability to find rapidly on the local market material such as cement, pipes, soap.
	3. Technical component	3. Ability to use appropriate technology according to locally available material, technical knowledge and cultural acceptability.
	4. Accessibility	4. Distance to water source and to latrines, access 24 hours/day or not.
Surveillance system	Capacity to ensure early detection and monitoring of outbreaks	
	1. Alert system within the community	1. Reaction capacity, (tele)communications.
	2. Surveillance system	2. Trained human resources, data management.
	3. Diagnosis, laboratory confirmation	3. Trained human resources, laboratory, supplies.
National and local authorities	1. Local governance systems	1. Camp management, detaining authorities, local authorities.
	2. Management	2. At all levels of intervention.
	3. Intersectoral coordination	3. Partnership, coordination meetings.

3. Assessment of the feasibility of an OCV camp

Elements to assess	Factors to consider	For example
Vaccines (currently prequalified OCV) + buffer	1. Availability of good-quality products, shelf-life	1. Possible production within a given timeframe.
	2. Timing to arrive on site	2. nternational and local transport.
	3. Regulatory approval	3. In the importing country, customs regulations, etc.
	4. Price	4. Currently up to US$ 8 per dose
Vaccines (potential new vaccines)	1. Availability of good-quality products	1. Potential manufacturers.
	2. Timing to arrive on site	2. International and local transport.
	3. Regulatory approval	3. Prequalification process.
	4. Ease of use/formulation	4. Single-dose, easy-to-use vaccine.
	5. Price	5. Inexpensive vaccine and related material.
Access	1. Roads, airstrips	1. Road conditions, distance.
	2. Security	2. Conflict, landmines, checkpoints, etc.
	3. Climatic conditions	3. Rainy season, earthquakes, etc.
Population	1. Size	1. To evaluate with precision.
	2. Target population	2. Criteria for selection (subgroups, vulnerability, etc); % of the population to reach; how to respect the targeting?
	3. Stability	3. Guarantee to have the same people for the two doses (limited movements in and out), accessibility to the population.
	4. Acceptability	4. No strong expressed opposition, cultural awareness, risk of social stigmatization?
	5. Strong social network	5. To inform and mobilize the community.
Logistics (for 10 000 people)[1]	1. Transport and storage capacity	1. International and local transport of vaccines and related material by truck, aircraft, etc., up to vaccination posts.
	2. Cold chain capacity	2. To be assessed carefully; usually difficult to find in sufficient space and volume.
	3. Equipment and supplies	3. Clean water in large quantity, paper, pens, cups, buckets, etc.
	4. Telecommunication	4. To maintain contact with and supervision of vaccination teams (telephone, radio, satellite telephones, e-mails, etc.).
	5. Waste management	5. Appropriate waste points, glass recycling facilities (usually difficult to find).

[1] For 10 000 people: total weight and storage volume of vaccine vials, buffer, plastic cups and water are about: 3700 kg and 8.1 m^3; without the water, weight is only 422.5 kg and volume 3.5 m^3.

Elements to assess	Factors to consider	For example
Resources	1. Human resources: number, training, training capacity	1 Vaccination teams, team leaders, supervisors.
	2. Financial resources	2 Vaccines, transport, per diem payments, cold chain, supplies, etc.
	3. Partners and coordination	3 Ministry of health, NGOs, local partners, community. Establish responsibilities and close monitoring throughout the implementation.
Outline of implementation plan	1. Well-defined target population	1 People with less access to safe water; people with poor sanitation facilities; people with limited access to health care.
	2. Detailed strategy, including realistic timing, and resources needed	
Monitoring capacity	1. Monitoring the implementation	1 Strong monitoring and close supervision needed.
	2. Monitoring the outpost	2 Vaccination coverage.
	3. Follow-up of the epidemiological and biological surveillance	3 Case control, number of vaccinated vs non-vaccinated people with confirmed cholera.

Remarks

- Each step of the decision-making process should be assessed carefully and each element linked with the next, as shown in the decision-making tree (Figure A1.1).
- The Global Task Force on Cholera Control, at WHO headquarters, will provide expertise and guidance whenever necessary. Decision-makers should not hesitate to contact the Task Force with any doubts or questions.
- A high level of political commitment by all stakeholders and national authorities is critical.
- If a decision is made to conduct a cholera vaccination campaign, water and sanitation programmes should be implemented before (or at least concurrently with) vaccination. A surveillance system –including laboratory capacity to diagnose cholera and basic health education for communities – should also be implemented before a mass cholera vaccination campaign is started.

Annex 2

Agenda

Introduction	
Opening and welcome address	*Dr Z. Hallaj*
Overview on the cholera situation worldwide and use of OCV in public health so far	*Dr C.L. Chaignat*
Session 1: Available Vaccines and New Developments	
Update on currently available OCV and vaccines under development and formulations	*Dr S. Wiersma*
Killed and live vaccines: pros and cons	*Dr D. Lewis*
Update on herd immunity and herd amplification	*Dr D. Sack*
Ongoing IVI cholera vaccine projects in Asia	*Dr L. von Seidlein* *Dr L. Jodar*
Session 2: Crisis Situations and Cholera Control	
Complex emergencies and natural disasters: definition and challenges; interagency committee and cluster approach	*Dr F. Del Ponte*
Risk assessment for cholera outbreaks	*Dr D. Legros*
Overview of surveillance systems and data gathering in complex emergency countries	*Dr J. Jabbour*
Water and sanitation for cholera control: what are the challenges?	*Ms C. Frazier*
Response to a cholera outbreak and cost involved	*Dr M. Henkens*
Session 3: OCV Use in Crisis Situations	
Cholera in complex emergencies: OCV an added value?:	
• Closed and open settings	*Dr M. Henkens*
• Detention facilities	*Dr P. Perrin*
Recent use of OCV in complex emergencies: Darfur, July 2004	*Dr N. Zagaria*

Session 4: Challenges for OCV use in Crisis Situations

Use of OCV in Aceh, Indonesia, March to August 2005	*Dr C.L. Chaignat*
Logistics of OCV mass vaccination : the case of Aceh	*Mr H. Supaat*
Challenges for mass vaccination campaigns using OCV	*Dr C.L. Chaignat*
Pakistan, the current crisis: interagency approach and challenges for cholera control	*Mr A. Musani*
Myths that won't die	*Dr F. Del Ponte*

Working group session: development of recommendations on the use of OCV in complex emergencies

Session 5: OCV Use in Endemic Setting

Out of country experience definition of endemicity: Country specific examples	
• West Bengal	*Dr S. Bhattacharya*
• Pakistan	*Dr A. Zaidi*
First demonstration project using OCV, Beira, Mozambique:	*Dr M. Lucas*
• feasibility and effectiveness after 6 months	
• effectiveness after 1 year (case–control study phase 2, Beira)	*Dr L. von Seidlein*
Vaccination strategies: EPI and other options for vaccination	*Dr N. Teleb*
Cost effectiveness of OCV use in endemic settings	*Dr D. Sack*

Working group session: development of recommendation for the use of OCV in endemic settings

Session 6: Availability of OCV and Pertinence of a Stockpile for Epidemic and Endemic Settings

Existing vaccine stockpiles and ICGM mechanism	Dr E. Bertherat
Availability and cost of current OCV	Mr B. Sjöstrand
The case for a cholera vaccine stockpile	Dr L. Jódar

Concluding remarks

Annex 3

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