

Purpose

This note provides guidance for UNICEF on the use of oral cholera vaccines (OCV) to implement the 2010 World Health Organization (WHO) recommendations on public health use of OCV¹. This note does not replace WHO guidance and recommendations but summarizes existing information on OCV and provides options for UNICEF to engage with governments, WHO and partners. The guidance will be updated accordingly with new WHO recommendations.

Summary

Oral cholera vaccines are safe, effective, and acceptable (see Annex A for details on OCV). They present an additional tool for cholera control to supplement, but not to replace, existing priority cholera control measures. With the September 2011 WHO prequalification of a newly manufactured cholera vaccine that is significantly lower in price (50% lower) and simpler to deliver than other cholera vaccines, - it has no need for buffer, has a smaller packed volume and has a vaccine vital monitor (VVM) - there is increased opportunity to use OCV, either pre-emptively or reactively. Furthermore, the International Coordinating Group (ICG) consisting of MSF, IFRC, UNICEF and WHO, is considering the establishment of an OCV stockpile for epidemic response.

UNICEF recommends engagement with governments, WHO and partners to consider OCV use pre-emptively in endemic, at-risk and humanitarian settings and reactively in outbreaks. In all contexts, the decision-making process must be based on a sound risk assessment.

Background

The incidence of cholera is on the rise, with more than 500,000 cases and 7000 deaths reported worldwide in 2011². However, these data are considered a significant underestimate; the actual burden of cholera is estimated to range anywhere from 1.4 million to 4.3 million cases worldwide, resulting in 28,000 to 142,000 deaths per year worldwide, among the 1.4 billion people at risk in endemic countries³. The trends in cholera globally are alarming. There is an increased frequency of large and protracted cholera outbreaks with high mortality, reflecting the weaknesses of existing mechanisms for prevention, early detection, control of spread and access to timely health care. Cholera has become entrenched in more countries in Africa, and it has recently returned to the Americas with ongoing transmission in Haiti and the Dominican Republic. A new strain of *Vibrio cholerae*, more virulent and causing a more severe clinical illness, emerged in 1992 and has now spread globally⁴. In addition, climate change and rapid and unplanned urbanization are increasing the pool of already marginalized

¹Cholera vaccines WHO position paper Weekly Epidemiologic Record (WER) No 13, 2010, 85, 117-128 <http://www.who.int/wer/2010/wer8513.pdf>

²Cholera 2011 Weekly epidemiologic record (WER) No. 31-32, 2012, 87, 289-304 http://www.who.int/wer/2012/wer8731_32.pdf

³Ali M, Lopez AL, You YA, Kim YE, Sah B, Maskery B, Clemens J. The global burden of cholera. Bull World Health Organization, 2012, 1;90(3):209-218A.

⁴Siddique AK, Nair GB, Alam M, Sack DA, Huq A, Nizam A, Longini IM Jr, Qadri F, Faruque SM, Colwell RR, Ahmed S, Iqbal A, Bhuiyan NA, Sack RB. El Tor cholera with severe disease: a new threat to Asia and beyond. Epidemiol Infect. 2010 Mar;138(3):347-52.

populations at risk⁵. Children under five bear the greatest burden of cholera in endemic areas, and account for about half of the estimated cholera deaths⁶. A marker of inequity, cholera targets the most vulnerable of at risk communities. These populations possess the poorest underlying health status, the least access to essential services such as safe water, sanitation, hygiene, health services and education messages, and they live in the most fragile settings prone to crises and global socio-economic fluctuations.

The 64th World Health Assembly (WHA) in 2011 highlighted this increasingly pressing situation and called for renewed efforts for cholera prevention and control. The WHA urged countries “to undertake planning for and give consideration to the administration of vaccines, where appropriate, in conjunction with other recommended prevention and control methods and not as a substitute for such methods”⁷.

Recommendations for UNICEF

UNICEF can play a critically important, supportive role in advancing the consideration of cholera vaccines as an additional public health tool in global, regional and national cholera prevention and control strategies. UNICEF Country Offices should engage with national counterparts and partners who may consider the introduction of OCV as part of the long-term strategy for cholera control and who may also propose the use of OCV in specific situations like humanitarian crises or outbreaks, in addition to the activities laid out in the Core Commitments for Children in Humanitarian Action (CCCs). Once the decision is taken to use OCV, UNICEF Country Offices can play an essential role in the implementation of vaccination campaigns.

General considerations for the use of oral cholera vaccines

This section provides information to help UNICEF appreciate why to use OCV, when (in what context) to consider their use and how to use them, including where and for whom, based on current WHO guidance and recommendations.

Priority cholera control measures should aim at (1) preventing the spread of cholera through strong disease surveillance and early warning, access to safe water, adequate sanitation, hygiene and food safety measures and (2) limiting mortality through early detection and timely and effective case management.

The use of OCV as an additional tool will vary according to the country and context; decisions on their use will be made by national health authorities supported by WHO and other partners. In any setting, initial consideration to use OCV should be based on:

- A sound risk assessment that clearly outlines cholera epidemiology and trends;
- The capacity of the community and national mechanisms to prevent and control outbreaks;
- The feasibility of conducting a cholera vaccination campaign and attaining good coverage;

⁵Background Paper on the Integration of Oral Cholera Vaccines into Global Cholera Control Programmes

http://www.who.int/immunization/sage/1_Background_Paper_Cholera_Vaccines_FINALdraft_13_oct_v2.pdf

⁶Deen JL et al. The high burden of cholera in children: comparison of incidence from endemic areas in Asia and Africa. PLoS Neglected Tropical Diseases, 2008, 2(2):e173. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2254203/pdf/pntd.0000173.pdf>

⁷Cholera: mechanism for control and prevention http://www.who.int/cholera/technical/Resolution_CholeraA64_R15-en.pdf

- The relevance of OCV with respect to competing public health priorities.

Documenting both the decision and outcomes of use or non-use of OCV will be vital to developing evidence-based guidance and strengthening recommendations for future OCV use.

Why vaccinate with OCV

The intent of OCV use is to both protect the individual who receives the vaccine and to reduce transmission and, consequently, the burden of disease in the community.

When to consider the use of OCV

There are effectively two contexts when OCVs can be used:

1. **Pre-emptive vaccination** of populations takes place **before** likely upsurges in cholera transmission or outbreaks in order to limit and reduce spread of the disease. Pre-emptive vaccination aims to:
 - *Contribute to the control of diarrheal diseases* in countries and communities where cholera is *endemic*⁸ with known cholera transmission occurring at predictable times and places, i.e., seasonal upsurges;
 - *Prevent a potential outbreak* in targeted populations and areas at risk for cholera outbreaks i.e., areas that lack essential services to prevent the spread of *Vibrio cholerae* in the environment, such as adequate clean water, sanitation and hygiene;
 - *Prevent a potential outbreak during humanitarian crises* where essential services to prevent the spread of *Vibrio cholerae* in the environment (adequate clean water, sanitation and hygiene) and health care are disrupted or destroyed, populations may be on the move or residing in crowded settings and the area is at risk for cholera outbreaks.
2. **Reactive vaccination** of populations occurs **after** the start of an outbreak and aims to limit mortality (protect the individual who receives the vaccine) and reduce the spread of the disease. Reactive vaccination aims to:
 - *Reduce spread to and limit mortality in a community at imminent risk* of outbreak extension but one that is either not yet or so far little affected by the current outbreak, i.e., neighbouring communities - across borders, or linked by river systems or water and sanitation systems.

An outbreak of cholera at the national level commonly consists of a succession of several outbreaks as it spreads through the country or across borders. Vaccinating communities in areas at imminent risk during such a succession would have greater impact than in areas where the transmission has already been active for several weeks or months. Many of the individuals in a community where there is active transmission may have already been infected with cholera even if they are asymptomatic. In fact, an estimated 80 per cent of infected

⁸Endemic cholera: WHO: the occurrence of faecal culture-confirmed cholera diarrhoea in a population in at least 3 of the past 5 years.

individuals will be asymptomatic but still shed the bacteria. This reactive strategy is particularly important in areas where response mechanisms cannot deliver typical cholera control measures^{9,10}.

The epidemiologic and contextual criteria for the use of OCV in epidemic settings should be carefully analysed as part of the decision-making process. Documentation and evaluation of impact of future use of OCV in various contexts will be critical to further refine the evidence-based decision making process.

How to deliver OCV

It is anticipated that OCV will be delivered to high-risk areas through mass vaccination campaigns, given two important considerations:

1. **Where to target mass campaigns:** Based on a thorough situational risk assessment, vaccination should target geographic areas and communities that are particularly vulnerable, especially marginalized populations, crowded and unhygienic settings, urban slums, refugee and displaced sites, and communities who lack access to safe water, sanitation and hygiene and health services.
2. **Whom the mass campaigns should target:** All people over the age of one year in the at-risk communities may benefit from receiving OCV. In endemic contexts, adults are likely to be already immune, so they may be of less value to include in the target population. In most contexts the following guidance applies:
 - **WHO recommends prioritising children as they have the greatest risk of death, particularly if resources are limited.** Such prioritisation may also have a greater impact in preventing transmission in the community.
 - **Target other groups with increased risk of death**, e.g., pregnant women, individuals with HIV, those with moderate or severe malnutrition and older populations, if resources allow.

Mass vaccination campaigns require community support, especially for selecting the target groups. This process requires dialogue with community leaders as well as a strong, carefully designed communication component that should address: continuation of hygiene and prevention behaviors, population perception of the risk of cholera, the introduction of OCV as a new vaccine, potential confusion with other mass vaccination campaigns such as polio, ineffectiveness against other diarrheal diseases, i.e., vaccinated individuals can still become sick with acute diarrhea.

3. **Additional feasibility considerations during large epidemics and humanitarian crises¹¹:** During an acute humanitarian crisis or large cholera outbreak, consideration of the use of OCV should not distract from the immediate priority of implementing lifesaving interventions to quickly reduce crisis-related excess mortality and providing basic lifesaving services related to health, water, sanitation, hygiene, food, shelter, and

⁹ Oral cholera vaccine use in complex emergencies: what next? WHO Meeting Report 2005

http://www.who.int/cholera/publications/cholera_vaccines_emergencies_2005.pdf

¹⁰ Ad hoc meeting of experts convened by WHO for cholera control in humanitarian emergencies 2010

¹¹ Oral cholera vaccine use in complex emergencies: what next? WHO Meeting report 2005

http://www.who.int/cholera/publications/cholera_vaccines_emergencies_2005.pdf

protection. A 2005 WHO meeting on the use of OCV in humanitarian settings, outlined the following considerations that require special attention in planning and conducting a two-dose vaccination campaign:

- Availability, arrival time and distribution of vaccines;
- Continuous access to at-risk populations to identify the most vulnerable groups, performance of a risk assessment and execution of a campaign with good coverage;
- Population movements (particularly for the second dose);
- Local supply and logistics constraints (including storage and cold chain capacity);
- Human resources constraints and access to trained staff;
- Prevailing security conditions.

The WHO-appointed Strategic Advisory Group of Experts (SAGE) Working Group on Vaccination in Humanitarian Emergencies is developing an updated framework for use of OCV in humanitarian settings for release in 2012-2013.

UNICEF's role as a supporting agency

At the Global and Regional levels, UNICEF can play a supportive role as a partner to WHO and key stakeholders to:

- Advocate for the most appropriate use of OCV in specific settings through an approach that is integrated with standard prevention and treatment interventions;
- Document decision-making processes as well as the effectiveness, feasibility and impact of mass campaigns in various contexts;
- Develop further guidance and tools on the use of cholera vaccines;
- Through Supply Division (SD), work with vaccine manufacturers to facilitate the supply of vaccines;
- Support the development and implementation a global OCV stockpile mechanism;
- Act as a member of the International Coordination Group (ICG) for the OCV global stockpile.

At the Country level, as part of its commitment to preparedness, UNICEF should support governments, WHO and partners to prevent, prepare for and respond to cholera through actions including effective coordination, preparedness and response planning, and the implementation of standard prevention and treatment efforts. In addition, UNICEF can engage in the development and implementation of OCV vaccination strategies with national authorities, WHO and partners to:

- Review the epidemiological situation of cholera at local level, including the historical endemicity, attack rate and case fatality rate of previous outbreaks and the extent of the current outbreak;

- Identify risk areas and communities for targeted vaccination (risk assessment) and build corresponding capacity needed at national and regional levels;
- Support the most relevant strategy, given local conditions, for the eventual introduction of OCV as a component of the national strategy for cholera control, and document the decision-making process;
- With SD, or through the potential OCV stockpile mechanism, source OCV from manufacturers, procure it, and distribute it to governments and partners;
- Procure and distribute other necessary supplies including cold chain equipment (linked to existing procurement systems through SD);
- Plan and conduct vaccination campaigns including logistics and capacity building (according to existing national immunization programs and systems);
- Conduct social mobilization for campaigns and monitoring;
- Document effectiveness, feasibility and impact of the use of OCV in various contexts.

How to access vaccines and technical support

For further information and technical support on OCV and decision making, please contact:

- Heather Papowitz: Senior Advisor Health – Emergencies, PD/NY, hpapowitz@unicef.org with cc to:
- Osman Mansoor: Senior Health Advisor (New Vaccines), PD/NY, omansoor@unicef.org

For further information on OCV procurement and supplies:

- Ana Balmes: Contracts Manager in Supply Division, Copenhagen, abalmes@unicef.org
- Ian Lewis: Contracts Officer in Supply Division, Copenhagen, ilewis@unicef.org

For further information on OCV procurement and supplies during humanitarian crises:

- Jens Grimm, Logistics Specialist in Supply Division, Copenhagen, jgrimm@unicef.org
- Jean-Cedric Meeus, Senior Emergency Supply Manager, Copenhagen, jcmeeus@unicef.org

Resources

- WHO Publication: “Oral cholera vaccines in mass immunization campaigns: guidance for planning and use” http://whqlibdoc.who.int/publications/2010/9789241500432_eng.pdf
- A three-step decision-making tool for the reactive use of OCV (to analyse risk, capacity to contain an outbreak, and feasibility of conducting a campaign) is described in Annex 1, pages 47-54 of the above WHO publication. http://whqlibdoc.who.int/publications/2010/9789241500432_eng.pdf
- Webinar: Cholera and Cholera Vaccines: an update for UNICEF <http://intranet.unicef.org/PD/CBSC.nsf/Site%20Pages/Page0201> (intranet) and <https://vimeo.com/45662328> (external) *password is response2012*.

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Annex A: Cholera vaccine specifications

Basic information: Oral cholera vaccines (OCV) are safe, effective, feasible and acceptable according to various studies on their use. There are currently two WHO prequalified OCV, Dukoral^{®12} and Shanchol^{®13}, that provide protective efficacy greater than 60 percent (> 60%) for at least two years (see table for dosing schedule). A booster dose is recommended by the manufacturer for both vaccines every two years (every six months in children 2 – 5 years old for Dukoral[®]). This recommended interval may change as a recently published study showed a 65 per cent protective efficacy of Shanchol[®] among adults during the third year of follow up¹⁴. Re-analysis of data of a Bangladesh trial that took place in the 1980s showed some evidence of extended protection to people not vaccinated, allowing for an additional benefit from large-scale vaccination of at-risk populations¹⁵. Both vaccines require a cold chain, and Dukoral[®] requires dilution with a buffer solution. Dukoral does not have VVM, but lab results indicate good heat stability. Research is underway for the use of a single dose of Shanchol[®] in clinical trials in India and for other vaccines that are more efficient for field use.

Cost effectiveness: A global investment case was conducted by the International Vaccine Institute (IVI) to provide evidence for investing in OCV production and use as part of a broader public health strategy for cholera control. The study concluded that in 15 years cholera vaccination could prevent up to 18 million cases and 600,000 deaths and would be “very cost effective” (using WHO definition of the cost/DALY \leq GNP/capita) particularly programs targeting children¹⁶. A study by the Diseases of the Most Impoverished Program used data on incidence, cost of illness and private demand for OCV from Beira, Mozambique, Matlab, Bangladesh, Kolkata, India and North Jakarta. Vaccination in all sites would be cost-effective, and programs for children (1-14 years old and 5-14 years old) would be “very cost-effective” in both Beira and Kolkata taking into account herd protection¹⁷.

Availability of cholera vaccines/global stockpile: The current annual production capacity is 2 million doses of each vaccine with a possible increase based on demand¹⁸. The creation of a stockpile of at least 2 million doses of OCV for outbreak control was recommended at the 2011 WHO consultation on OCV stockpile and confirmed in a 2012 WHO consultation. A global stockpile could act as a “gateway” to make the vaccines more readily accessible for field use, increase efforts towards surveillance, increase the demand and supply, motivate manufacturers and provide experience for deploying vaccines and evaluating the impact of vaccination to control

¹²Jertborn 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.

¹³Trach 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.

¹⁴Sur D, Kanungo S, Sah B, Manna B, Ali M, et al. Efficacy of a Low-Cost, Inactivated Whole-Cell Oral Cholera Vaccine: Results from 3 Years of Follow-Up of a Randomized, Controlled Trial. *PLoS Negl Trop Dis*, 2011, 5(10): e1289.

¹⁵ Ali M et al. Herd immunity conferred by killed oral cholera vaccines in Bangladesh: a re-analysis. *Lancet*, 2005, 366:44–49.

¹⁶ http://www.who.int/immunization/sage/SAGE_April_2011_cholera_investment_case.pdf

¹⁷Jeuland M, Cook J, Poulos C, Clemens J, Whittington D, DOMI cholera economics study group. Cost-effectiveness of new-generation oral cholera vaccines: a multi-side analysis. *Value in Health*, 2009, 12(6):899-908.

¹⁸WHO Consultation on oral cholera vaccine (OCV) stockpile strategic framework: potential objectives and possible policy options meeting report. 6-7 September 2011. Geneva, Switzerland

outbreaks. UNICEF is a member of an International Coordinating Group (ICG) for the management of the stockpile.

Summary of studies: Research conducted in endemic settings (Vietnam 1998¹⁹, Beira-Mozambique 2003-2004²⁰, Zanzibar 2009), in stable refugee camps (Uganda 1997²¹, Darfur 2004²²), in emergencies (Aceh 2005²³) and during cholera outbreaks (Micronesia 2000-2001²⁴, Hanoi 2008²⁵) provide broad indication that, overall, the use of OCV is feasible and acceptable as an additional public health tool to prevent the spread of cholera in synergy with traditional control measures, with some lessons and limitations as outlined below.

In 1998, in Hue, Vietnam, mass campaigns took place at schools, community health centers, government buildings and homes of group leaders. Coverage was 84 per cent for the first dose and 79 per cent for the second dose. The wastage rate was 10 per cent. The vaccine effectiveness was estimated at 76 per cent. Since 1998, yearly campaigns target children 1-15 years old and are conducted before the peak cholera season. Pre-emptive vaccination also takes place during natural emergencies, such as floods.

In Beira, Mozambique, a cholera-endemic neighbourhood was vaccinated using Dukoral[®] in December 2003 and January 2004. The vaccination campaign was preceded by information campaigns that included door-to-door visits. Vaccination teams inoculated an average of 609 persons per day. Overall, more than 98,000 doses of vaccine were administered during the two rounds. Response during the first round was strong and many of the people vaccinated were from outside of the targeted area. The vaccine coverage was 57 per cent. The vaccination campaign was shown to be feasible, although the vaccine presented some logistical challenges.

Nearly 44,000 refugees living in camps were targeted for cholera vaccination in Northern Uganda in 1997, using Dukoral[®]. Acceptance among this stable population was high, with coverage estimated at 83 per cent for the first dose and 76 per cent for the second dose. Logistical issues included the large amount of cold storage space required. Cholera vaccination campaigns were also conducted in two stable camps for internally displaced persons in Southern Darfur in 2004. The time from initial planning to completion of the second round was seven weeks. More than 40,000 people were fully immunized with two doses of Dukoral[®], with estimated vaccine coverage of 88 per cent. The organizers received strong support from the residents and community leaders.

¹⁹Vu DT, Hossain MM, Nguyen DS, Nguyen TH, Rao MR, Do GC, Naficy A, Nguyen TK, Acosta CJ, Deen JL, Clemens JD, Dang DT. Coverage and costs of mass immunization of an oral cholera vaccine in Vietnam. *J Health Popul Nutr.* 2003, 21(4):304-8.

²⁰Cavailler 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-

<http://fieldresearch.msf.org/msf/bitstream/10144/18822/1/feasibility%20of%20a%20mass%20vaccination.pdf>

²¹Legros D, Paquet C, Perea W, Marty I, Mugisha NK, Royer H et al. Mass vaccination with a two-dose oral cholera vaccine in a refugee camp. *Bull World Health Organ* 1999; 77(10):837-41.

²²Chaignat CL, Monti V, Soepardi J, Petersen G, Sorensen E, Narain J. Cholera in disasters: do vaccines prompt new hopes? *Expert Rev Vaccine* 2008; 7(4):431-35.

²³Chaignat CL, Monti V, Soepardi J, Petersen G, Sorensen E, Narain J, Kieny MP. Cholera in disasters: do vaccines prompt new hopes? *Expert Rev Vaccines.* 2008, 7(4):431-5.

²⁴Calain P, Chaine JP, Johnson E, Hawley ML, O'Leary MJ, Oshitani H, Chaignat CL. Can oral cholera vaccination play a role in controlling a cholera outbreak? *Vaccine.* 2004, 22(19):2444-51.

²⁵Anh DD, Lopez AL, Thiem VD, Grahek SL, Duong TN, Park JK, Kwon HJ, Favorov M, Hien NT, Clemens JD. Use of oral cholera vaccines in an outbreak in Vietnam: a case control study. *PLoS Negl Trop Dis.* 2011, 5(1):e1006.

Following the tsunami in 2005, mass cholera vaccination campaigns using Dukoral[®] vaccine were conducted over a six-month period in Aceh among internally displaced persons. Logistics were made difficult by high level of population movement, damaged roads, depletion of local health workers, security problems and limited cold chain capacity in the area. More than 54,000 persons received both doses, for an overall coverage of 69 per cent, but at significant cost and logistical challenges.

Three experiences of reactive use of OCV during cholera outbreaks have been documented. On the Pohnpei Island of Micronesia in 2000-2001, the single-dose live-attenuated CVD 103-HgR vaccine (Orochol[®], which is not marketed anymore) was used in an effort to control an outbreak which was spreading across the archipelago. Vaccine effectiveness was estimated at 79.2 per cent. In 2007–2008 in Vietnam, the occurrence of cholera outbreaks in the capital, Hanoi, prompted authorities to conduct a two-dose vaccination campaign using the Vietnamese killed OCV (same as Shanchol[®] vaccine) in two districts. The vaccine effectiveness was estimated at 76 per cent. A mass vaccination campaign using Shanchol[®] was conducted in Guinea Conakry in the district of Boffa (total population 162,190 inhabitants) from mid-April to mid-May 2012. The campaign was organized by the Ministry of Health and Médecins sans Frontières (MSF), with the support of the Agence de Médecine Préventive (AMP). The first cases of cholera had been confirmed in the district in early February 2012, two months before the beginning of the rainy season, and were still increasing in March when the decision to vaccinate was taken. The campaign targeted the entire population over 1 year of age. The vaccine coverage for the two doses reached 77 per cent of the target population (90 per cent for the first round). The last case of cholera in Boffa was reported in early May 2012²⁶.

The cost of delivering the vaccines in country (not including the vaccine itself) was in the range of \$0.50 to \$0.70 per fully immunized person in the various settings, with the notable exception of Aceh (\$8.15 per fully immunized).

WHO Pre-qualified Vaccines	Dukoral [®]	Shanchol [®]
Type of vaccine	Killed whole cell <i>V.cholerae</i> O1 plus recombinant B subunit of cholera toxin (WC/rBS)	Killed whole-cell bivalent vaccine (O1 and O139); no B subunit
Age	From two years of age; no upper age limit.	From 1 year of age; no upper age limit.
Dosing	2 doses given orally 1-6 weeks apart. 3 doses in children 2 – 6 years old.	2 doses given orally 2 weeks apart. Booster dose after 2 years

²⁶ 11 June 2012 (<http://www.nature.com/news/cholera-vaccine-deployed-to-control-african-outbreak-1.10801>)

	Booster dose after 2 years.	
Packaging	3ml single dose vials each with a sachet of sodium bicarbonate buffer	1.5ml single dose vials
Buffer	Dilution in 150ml of water (75ml for children 2-5 years) mixed with buffer	No buffer needed
Protection/efficacy	Protection is 1 week after 2 nd dose. 85-90% protection at 6 months in all age groups and 62% at 1 year in adults	Earliest onset of protection 7-10 days after 2 nd dose Provides 67% protection over 3 years
Adverse effects	No significant adverse effects reported.	No significant adverse effects reported.
Storage and Cold chain	3 year shelf life at 2-8 C and is stable for 1 month at 37C. No VVM. Packed volume per dose: 136cm ³ (In 2-dose pack; also available in 20-dose pack)	2 year shelf life at 2-8C VVM 14 Packed volume per dose: 16.8cm ³ (In 35-dose pack)
Manufacturer	Crucell	Shantha, a Sanofi Company
Production capacity	2 million doses per year	2 million doses per year but plans on 10 million with additional facilities
Countries licensed	Licensed in 60 countries	India
Estimated prices per dose*	Crucell: EUR 3.6 to 7.2	Shanta: USD1.85

*Estimated vaccine prices only for public sector, a tender process will be required to fix prices.