

MEETING REPORT

3rd Meeting of the Initiative against Diarrheal and Enteric diseases in Asia (IDEA), Tagaytay City, the Philippines

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Version 4

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ABSTRACT

The Initiative against Diarrheal and Enteric diseases in Asia (IDEA) is a unique mix of clinicians, public health and policy experts, scientists, and other health professionals from eight cholera endemic countries of Asia, sharing the common goal of cholera elimination from their respective countries, and thereby eventually from the region as a whole. IDEA holds meetings annually in different cholera endemic countries of Asia. So far, it has held three such meetings. The third and latest one was held in Tagaytay City in the Philippines in January 2014. The major focus of this year's meeting was Advocacy and Policy. Two workshops were held, one on each day, solely dedicated to these topics. A major outcome of these workshops was the emergence of an Advocacy document and a Policy Brief. These will be very useful for sensitization of the policy makers in the respective member countries. In some cases, these would have to be slightly modified in order to suit specific country situations and needs. This 3rd Meeting of IDEA, held in the Philippines, is represented in this report for the benefit of those who are interested in the cholera scenario in the region and the current ongoing efforts to eradicate this scourge from the cholera endemic countries of Asia.

IDEA is a unique, independent, multidisciplinary and multinational group of Asian health professionals involved in the surveillance, control and prevention of cholera and other enteric diseases. This initiative is hosted by the Fondation Mérieux, a non-governmental organization based in Lyon, France (www.fondation-merieux.org). Its mission is to participate and contribute to effective disease prevention and control efforts in Asia. It holds meetings annually in Asian countries that are generally endemic for cholera. So far, it has held three meetings, the first one in Chiang Mai (Thailand) in 2011, the second one in Yogyakarta (Indonesia) in 2012, and the third one in Tagaytay City (Philippines) in January 2014. This meeting report will discuss about the latest meeting i.e. the third in the series.

The 3rd IDEA meeting took place in Tagaytay City, approximately an hour's drive from Manila, the capital of the Philippines. Representatives from a total of eight Asian countries participated in the meeting. These included the Philippines (the hosts), Bangladesh, India, Indonesia, Myanmar, Nepal, Pakistan, and Sri Lanka. Importantly, Thailand could not participate like other years due to the ongoing socio-political unrest prevailing in the country at the time. Each country and invited organizations and partners gave presentations on the current situations regarding cholera and their activities in this field. All presentations are available on the IDEA Asia website (<http://www.idea-asia.info>).

DAY 1 (January 14)

While Drs. Luc Hessel (General Secretary) and Catherine Dutel from the Fondation Mérieux welcomed everyone to the meeting, all the participants introduced themselves to the gathering. This was followed by Sara Fröjdö, from Alcimed, the agency supporting the organization of the meeting, who gave a brief introduction to the objectives of the meeting, organization and agenda and Dr. Marie Claude Bonnet's comments on Fondation Mérieux. (see Agenda in Appendix 1)

Then Luc Hessel updated the participants on the latest international cholera news since the last meeting and about the previous IDEA Africa meeting,

The second session on "Cholera Vaccination and Prevention News" was dedicated to presentations from invited organizations and partners sharing latest information on their activities against cholera, especially regarding the cholera vaccination introduction and stockpile.

DOVE (Delivering Oral Vaccine Effectively): Anna Lena Lopez

After highlighting the global burden of cholera, as well as the WHO statement on oral cholera vaccines (OCV), she touched upon the OCV timeline. She highlighted the fact that although >29 million doses of OCV had been given, there was still a very slow uptake of the vaccine. She dwelled on the various factors that impacted on this slow uptake. She then went on to talk about DOVE *per se*, how it was organized, who were the key stakeholders, its major objectives, as well as implementation aspects. She indicated the countries in Asia where OCV had been used. Then she highlighted a very interesting fact with reference to the

contrasting epidemiology of cholera in Africa and Asia. She concluded her talk by stressing on the fact that the use of OCV will depend on the intelligent use of the vaccine.

WHO: Marie Claude Bonnet, Fondation Mérieux, on behalf of Dr. A. Costa, WHO Geneva.

The talk was centered around the WHO EMRO-Strategic Framework for Cholera Prevention and Control, especially the international stockpile of OCV for the years 2013-14. After giving a brief background on the available OCVs, she went on to describe the International Coordinating Group (ICG) on the OCV stockpile. The various areas discussed included history and mission, objectives, and basic principles. She went on to discuss about the OCV stockpile – objectives, and OCV-ICG mechanisms and their components. She also talked about forecasting and storage in relation to ICG stock management. The other aspects that were discussed included ICG applications, ICG decision-making process, epidemiological criteria, minimum requirements to access the stockpile, revolving fund mechanism including an update on fundraising, and the OCV stockpile budget. In the conclusion, she did not forget to mention about monitoring and evaluation, as well as the ICG supporting tools, including the various guidelines.

IVI (International Vaccine Institute): Yanghee Kim from the IVI, South Korea

The third talk provided updates on OCV studies at the IVI. Firstly, she gave a list of the clinical research portfolio of IVI. These included the Phase III study (Kolkata, India): 5-year efficacy results; boosting trial (Kolkata, India); dosing interval trial (Kolkata, India); and the single dose trial (Dhaka, Bangladesh). The objective of the phase III study in Kolkata, India was to assess the protection of a two-dose regimen of an OCV against cholera episodes that were severe enough to require medical attention. The study was double-blinded, cluster-randomized, and placebo-controlled. Two 1.5ml doses were given 14 days apart. Participants were >1year of age and not pregnant. Surveillance was passive, which was carried out at study sites and local hospitals. The primary analysis involved the evaluation of vaccine protection against *V. cholerae* O1 diarrhea with onsets from 14 days to 5 years following receipt of the second dose, in all persons who received two complete doses. There was a two-thirds reduction in cholera cases among vaccinees one year of age and older. Protection was sustained for 5 years (Bhattacharya et al., 2013). The study did not detect differences in protection by age at immunization or year of follow-up, but the low efficacy in one to five year olds may suggest that the vaccine is less protective in less than five year olds. The limitations included that 95% of cases were due to a single strain, O1 Ogawa, with no cases of O139. Study was conducted in endemic population and immunity is likely induced by natural exposure and vaccine immunogenicity; and generalizing to epidemics is difficult. While the study did not detect differences by age group or by the year of follow-up, the study was not designed to evaluate these putative differences. The study did not evaluate vaccine efficacy for mild or asymptomatic cases. Then she talked about the boosting trial, also carried out in Kolkata, India. She highlighted the fact that killed vaccines demonstrated waning immunity and therefore a booster dose was required to maintain immunity. Based on expected waning of vibriocidal titers the modified, killed, bivalent OCV,

is expected to require a booster or re-immunization with two doses. Phase III evaluation of this 2 dose OCV demonstrated protection in endemic populations for 5 years. One of the objectives was to determine if one or two doses of OCV administered to a previously immunized cohort elicits similar immune responses to those achieved by primary immunization. Another objective was to confirm the safety of one or two dose boosting regimens of OCV in healthy adults and children. The study design was open label controlled trial (n= 426); allocated into 3 groups. The public health implications of the study were that the potential for a single dose boosting regimen could help to ease logistical challenges faced in introducing cholera vaccines in cholera endemic areas. The data suggested that a single dose boosting regimen could be given every 5 years and boost titers similar to those receiving a primary series in cholera endemic regions. However, a shorter period should be considered for children 3 years and younger. Yanghee then went on to talk about the dosing interval study, which was again carried out in Kolkata, India. She indicated that the absence of a boosting response after a 14 day interval with the two-dose regimen of the modified killed WC-OCV raises the possibility that a longer dosing interval may be required to observe a boost in the immune response. The primary objective was to analyze vibriocidal immune responses between the 14 and 28 days schedules. Secondary objective was to confirm safety in the study population. Participants included healthy children aged 1-17 years (n=178); healthy, non-pregnant adults aged 18 years and above (n=178). The study design was individually randomized, double-blinded and placebo-controlled. The public health implications were that the vaccine was safe and immunogenic and safe if given in a 28 day interval as well. With no difference in immunogenicity results between the two schedules, national program could entertain monthly dosing to ease logistical requirements in endemic and/or epidemic settings. Yanghee then went on to speak about the single dose trial currently being carried out in Dhaka, Bangladesh. The trial is an individually randomized, placebo-controlled trial to measure the protection conferred by a single-dose regimen of bivalent, killed, whole cell OCV (Shanchol™). A study in Kolkata (Kanungo et al., 2009) indicated that 65% adults (n=77) and 87% children (n=77) had \geq 4-fold rise in serum vibriocidal antibody titer after a single dose of the vaccine. This hints that the vaccine could be protective after a single dose. The primary objective of the study is to evaluate the protective efficacy of a single dose regimen with onset of days to 6 months (180 days) after dosing. There were a number of secondary objectives, including, protective efficacy over 24 months after dosing against culture-proven *V. cholerae* O1/O139 diarrhea with or without severe dehydration detected in treatment centers; protective efficacy over 24 months after dosing against acute watery diarrhea with or without severe dehydration detected in treatment centers; serum vibriocidal antibody responses; safety up to 28 days following dosing. The participants included healthy, non-pregnant residents of selected ward, aged 12 months and above. The study design involved a two-arm, individually randomized, double-blind, placebo-controlled trial (n= \sim 204,438). The dosing schedule has been completed. The public health implication of the study is that a single dose of the vaccine could lower the costs and the ease of administration substantially.

Shantha Biotech: Dr. Naveena Aloysia D'Cor

Shantha Biotech, a Sanofi Company is producing the already licensed and WHO-prequalified OCV, Shanchol™. The various aspects of Shanchol™, including product profile, clinical update and product update were presented. In the product profile, she indicated that Shanchol™ was a killed bivalent (O1 and O139) whole cell OCV. The vaccine consisted of a beige white turbid liquid suspension, which was indicated for active immunization against *V. cholerae*. It can be administered to anyone above the age of 1 year. She indicated that immunization studies in infants less than 1 years was being planned. For preventive immunization, 2 doses (1.5 ml each) was required at an interval of 2 weeks. Onset of protection would be expected to commence 7-10 days after the second dose. Shelf life of the vaccine is 30 months. In the clinical update Dr. D'Cor indicated that the protective efficacy of Shanchol™ lasted up to 5 years. She touched upon the 5 year cumulative efficacy of the vaccine. Talking about safety and efficacy, she cited the example of the phase IV study in India. Here, she made historical comparisons with previous studies. She also talked about the 14 day vs. 28 day dosing interval study of Shanchol™. She also highlighted the safety and immunogenicity of Shanchol™ in the randomized, double-blind, controlled trial carried out in Ethiopia. Talking about herd protection, she highlighted the study in the slums of Kolkata, India (Ali et al., 2013). She went on to describe a transmission model that showed the various possibilities of herd protection (Longini et al., 2007). She also cited the successful implementation of OCV programs in Haiti, both in urban areas (Rouzier et al., 2013) as well as in rural areas (Ivers et al., 2013). She also indicated that the Shanchol™ vaccine was successfully used in Africa as a first outbreak response. This study, in Guinea, first showed Shanchol's potential in mass vaccination campaigns in response to an outbreak (Luquero et al., 2013; Ciglenecki et al., 2013). In the product update, Dr. D'Cor talked about the temperature stability of Shanchol™. Controlled Temperature Chain (CTC) stability study indicated that Shanchol™ can be kept at temperatures of up to 40°C for a single period of up to 20 days prior to administration. The results have been presented to and accepted by WHO. She concluded her talk by speaking a little on the WHO Stockpile. She indicated that a stockpile is being established to fulfill the WHA resolution requesting the Director General of WHO to consider using the OCV in low income countries, for 2 million doses per year for 2 years. This stockpile will make OCV available for use during outbreaks and emergency situations. She also stressed the fact that Shantha had been granted the WHO order in July 2013, to provide required Shanchol™ doses for this stockpile. Dr. D'Cor's talk signaled the end of the session, which was followed by a lunch break, lasting till 1.30 PM.

Country Presentations

Following the lunch break, Luc Hessel gave an update on the roadmap and action plan that was initiated during 2012-2013. All the IDEA members gave their inputs and suggestions in this regard. This was followed by an information-sharing session, where the various experiences and initiatives led by IDEA members were shared with the house. The countries were encouraged to share information, actions, experience around key themes in order to prepare and nourish the working sessions on advocacy and policy. Each country was asked

focus its presentation on elements/initiatives important to consider for advocacy and policy and on the 3 following themes: (i) Water and sanitation; (ii) Surveillance system (epidemiology) and anticipation of events; and (iii) Vaccine introduction

Philippines:

The first talk from the Philippines was by Dr. Ruth Alma A. Ramos, which was entitled "Resurgence of Cholera in Basag, T'boli, South Cotabato, Mindanao, Philippines, 2013". She indicated that there was an outbreak of cholera in the southern tip of island nation in an area known as South Cotabato. As of May 28, 2013, there were 98 cases and 2 deaths. On June 3, 2013, a team of experts were sent from the Field Epidemiology Training Program (FETP) in Manila to investigate. The objectives of the investigation included (i) determination of the existence of an outbreak, (ii) identification of the source and mode of transmission, (iii) identification of the risk factors for the occurrence of cholera, (iv) recommendation of control and preventive measures. T'boli in South Cotabato had a population of 79,175 and consisted of 25 villages. One of these villages, Basag, had a population of 7,783 and consisted of 12 sub-villages, where there was a recorded cholera outbreak in 1996. The methods involved descriptive studies, including review of records, interview of cases, interview of key informant, environmental survey as well as laboratory investigations such as rectal swabs and examination of water samples. A case control study (1:2) unmatched was also carried out. Case definitions for suspect case, confirmed case and control case were established. A suspect case was defined as "a previously well resident of village Basag, T'boli with ≥ 3 episodes/day of watery diarrhea with or without any of the following: abdominal pain, nausea and vomiting from May 8-June 3, 2013". A confirmed case was defined as "a suspect case positive for *Vibrio cholerae*". A control case is defined as "a well individual negative for *Vibrio cholerae*". The investigation findings revealed incomplete medical records. Chlorination of water sources starting 22nd May, 2013 subsequently reduced the number of cholera cases (n=103) significantly. The cholera cases were slightly more in females than in males (n=103). Symptomatically, diarrhea was the predominant symptom (100%), followed by other symptoms such as abdominal pain (30%), vomiting (25%) and nausea (9%) (n=103). The cholera attack rate (May-June, 2013) was segregated by sub-village (n=103). It was found that the highest attack rate (5-8 per 100 population) was in Glungga, located to the East of Basag proper, where the attack rate was 1-2 per 100 population, as was in Tambag and Batotitik. The key informant interview revealed that in 1996 following an outbreak of cholera, two spring boxes were constructed, one in 1996 and the other in 1998. However, these lacked maintenance. Following this, the Local Water System Association was organized in 2010. Coming back to the present outbreak, importantly, in the first two weeks of May, 2013 there was heavy rainfall, leading to the mixing of water from the leaking water pipes, communal faucets, coupled with open defecation, absence of proper sanitation, led to the cholera outbreak. Three (7%) out of 46 stool samples were positive for *Vibrio cholerae* Ogawa El Tor. Water analysis revealed that 7 (88%) out of 8 samples were positive for *Aeromonas* sp. Importantly, the number of risk factors were substantial. The FETP expert team concluded that there was a resurgence of cholera in the village Basag, where

children below the age of 10 years were the most commonly affected. The CFR was 2%. The major reasons for the outbreak was lack of access to safe water and poor hygiene practices. The actions taken included (i) treatment and management of cases, (ii) distribution of aquatabs to all households, (iii) chlorination of water sources, and (iv) provisions of medicines and other supplies. The major recommendations that emerged included (i) to continue case finding and treatment of cases; (ii) to conduct health education campaign; (iii) to conduct community mobilization on good environmental sanitation practices; (iv) to rehabilitate the village water system; (v) to reactivate the functionality of the Local Water System Association; (vi) to allot funds for the construction of toilet facilities. In order to bring about this public impact, the Government of Philippines had spent USD 11, 600. Following implementation of the various interventions, the cholera cases completely disappeared from July onwards.

The second talk from the Philippines was jointly presented by Dr. Maria Liza Antoinette M. Gonzales, Dr. Anna Lena Lopez, Dr. Lino Y. Macasaet. The talk was entitled "Philippine Cholera Situation: 2013 Updates". The talk began with metropolitan Manila, and the two private water concessionaries that serviced the city. One was the Manila Water Company, which served the Eastern zone; and the other was the Maynilad Water Services for the Western zone. The provinces were supplied by the Local Water Utilities Administration. There were plans for the establishment of water districts in provincial cities and municipalities. There were also plans for provision of level II service (communal faucet system) through the Rural Waterworks and Sanitation Associations (RWSAs) in areas where Level III systems (individual household connection) were not feasible. They then highlighted the access to water 2002-2011; at the National level it improved 92.4% with piped water reaching 42.7% premises. Then they talked about sanitation 2002-2011; at the national level there was total improvement 74.2%; open defecation dipped to 7.7%. Talking about surveillance, they indicated that the main investigative unit for surveillance and outbreak investigation of the Department of Health (DOH) was the National Epidemiology Center. Other bodies that fell within the purview of DOH surveillance included Philippine Integrated Disease Surveillance & Response (PIDSR) and the Events-based Surveillance & Response (ESR). Other local Government counterparts included the City Epidemiology Surveillance Unit (CESU) and the Municipal Epidemiology Surveillance Unit (MESU). They also presented cholera cases by region for the years 2008 to 2013. Importantly, for the year 2013, there were a total of 3366 cases and 16 deaths, which on average was lower than the other years, with the exception of 2008, where the figures were even lower. Next, they talked about the DOH outbreak response and mitigation measures, which included stockpiling of essential commodities for outbreak response in all the 17 regions of the country. These essentially included water purification for outbreak areas, rapid point-of-care diagnostics, as well as therapeutics. Their talk ended with an encouraging note on vaccine introduction. It was indicated that a Technical Working Group had been formed in early 2013, which was composed of public health specialists, professors from the medical academy and clinicians to make a draft guideline for OCV use in an outbreak scenario. They revealed that Shanchol™ had been included in the Philippine Drug Formulary, which would enable government agencies to purchase the

vaccine. They ended with a piece of good news that Sanofi Pasteur had donated 4,000 vials of OCV for use in Tacloban, Leyte.

Bangladesh:

The Bangladesh presentation was entitled “Cholera Burden in Bangladesh” and was presented by Prof. Mesbah Uddin Ahmed. He began his talk with a heart-warming slide representing his country “beautiful Bangladesh”. He dwelled on this slide for a couple of minutes, then moved onto the major aspects of his presentation. He first presented all the major health parameters such as neonatal mortality rate, infant mortality rate, maternal mortality rate, as well as the health expenditure based on 2011 figures. He stressed on the fact that Bangladesh was a tropical, river-based and highly dense country, supported by some facts and figures. He then went on to cite some of the reasons why Bangladesh was an easy target for cholera. He indicated that seasonal rainfall and floods result in cholera outbreaks, almost on a regular basis. Importantly, there are many sources of unhealthy drinking and household water, as well as unhealthy housing and unsafe toilets. With reference to cholera epidemiology, he indicated that the estimated annual 450,000 cholera cases in Bangladesh was based on disease surveillance data from icddr,b and disease outbreak data from the Institute of Epidemiology, Disease Control & Research (IEDCR). He went on to indicate that the diarrheal hospital of icddr,b estimates about 300,000 severe cholera case hospitalizations each year. Importantly, for every hospitalized case of cholera, there are usually 3 more cases in the community, giving 1,200,000 cholera cases annually. Continuing on the same topic of cholera epidemiology, he indicated that cholera affects all age groups with the majority of fatal cases occurring in children, adolescents and old people. Most of the deaths happen even before reaching any healthcare facility. Overall, cholera is both endemic and causes epidemics in Bangladesh. Case fatality due to cholera is low, but morbidity is still too high in the country. After speaking briefly on the risk factors for cholera epidemics, he went on to highlight the preventive measures. He indicated that public health facilities were being improved by ensuring safe drinking water, improved sanitation, as well as fly control measures. Coupled with this, there were efforts to raise public awareness through campaigns on using proper sanitation, hand washing and maintaining personal hygiene, drinking safe water, cleanliness in food preparation, as well as methods and importance of early detection of cholera cases. He also indicated that there had been effective initiatives from the government, healthcare providers as well as institutions, including treatment facilities at local health authority, and effective reporting to higher authority. There has been heightened preparedness to combat cholera epidemics by way of preparing effective infrastructures; collaboration between government, NGOs and other healthcare providing organizations; as well as investigation of source of infection. Importantly, there is also vaccination of high-risk people. He then went on to highlight the current measures in force for cholera management. He indicated that diarrheal disease management was in line with national guidelines that supported a communication plan to induce behavioral change. He also highlighted the fact that oral rehydration therapy (ORT) corners with designated beds have been established in all public hospitals. Several NGOs were also involved in raising the awareness and use of ORS in combating diarrheal diseases. Regarding water and sanitation, a number of large

donor-supported projects were being implemented to improve population access to safe water and adequate sanitation. He also stressed that paramedics were being trained to provide support for diarrheal cases; healthcare facilities with proper infrastructure were being developed; health education coupled with mass education was being implemented at the grassroots level as well as in schools; and access to proper sanitation was being implemented. He then went on to talk about cholera immunization in Bangladesh. He indicated that although cholera vaccine was not available in Bangladesh, it was well on its way towards licensure. A feasibility study on introduction of double dose cholera vaccine was successfully conducted using the national immunization system of Bangladesh, using 'Shanchol' OCV and was completed in April 2011. He also indicated that the 3rd cholera vaccine feasibility study with single dose OCV started on 11th January 2014. He highlighted the fact that a high level consultative meeting with the Health Minister of Bangladesh regarding enteric diseases in general and cholera in particular had taken place. Before concluding, he indicated that dilemma still remained with reference to the actual number of patients who actually sought proper hospital care. He cited a study where the majority of under-five cholera cases were treated with home-based remedies, and only 6% sought care in the public sector. He concluded by stressing that cholera was a real problem in Bangladesh, and time had come to pay attention to this scourge and to institute preventive measures for its control.

India:

The India presentation was made by Dr. Kaushik Bharati with important inputs and personal experiences from Prof. G. Balakrish Nair. The talk was entitled "Why is cholera vaccine not used in India?", which was a rather thought-provoking title. Since the disease existed; the vaccine was available, yet not used; this was indeed an enigma. The presentation tried to explore why the vaccine was not used in India. Dr. Bharati first discussed the current classification of *Vibrio cholerae* and the derivatives of the El Tor biotype. He then went on to talk about the cholera pandemics and their causative biotypes. He also compared the proportion of severe cholera in the two biotypes i.e. classical and El Tor. From the clinical spectrum of *V. cholerae* infection, particularly with reference to stool characteristics, the classical rice water stool is present only in case of severe cholera cases, while in the majority of mild infections, the stool is usually loose or watery. The National Health Profile of India, 2012 (Central Bureau of Health Intelligence, 2012) showed that there were a huge number of acute watery diarrhea cases, whereas the number of cholera cases was comparatively miniscule. Even, states like Odisha, which was known to be cholera-endemic, did not contain a single case of cholera, which was rather strange. Dr. Bharati believed that the huge figures for acute watery diarrhea, particularly in places like Odisha, where the numbers touch nearly a million, mild cases of cholera could actually be lurking within these figures. He then went on to talk about Shanchol™, the OCV that is the only cost-effective vaccine currently available. It was a two dose vaccine, which has been licensed in India in February 2009 and WHO prequalified in September 2011. Cholera experts like Prof. Nair felt that there was a need to popularize the vaccine, particularly amongst the medical fraternity. Prof. Nair, at this stage, recounted his personal experiences to the audience. He indicated that after delivering the talks, he was bombarded with

questions like “Why have we made a vaccine against a disease that doesn’t exist?” or “Does the disease cholera exist in India?” and such like. Importantly, these questions were not from lay people, but from qualified doctors. This just goes to show that cholera has not only been wiped from the Public memory, but also from the physician’s psyche. Dr. Bharati then went on to address the questions (i) “How much cholera do we really have?” vis-à-vis (ii) “How much do we report?”. After analyzing data submitted to WHO (Kanungo et al., 2010) with data (personal communication, T. Ramamurthy) from a single hospital (Infectious Diseases Hospital), it was found that the two sets of data were comparable, indicating strongly the calamitous problem of under-reporting from India. Looking at the aggregated distribution of reported cholera cases over a span of 10 years i.e. 1997-2006 (Kanungo et al., 2010), it was evident that most of the states reported cholera cases, with the exception of a few that didn’t have a surveillance system in place. He then indicated the statewise highest number of cholera outbreaks over a span of 10 years (Kanungo et al., 2010); the states exhibiting highest number of outbreaks being West Bengal, Maharashtra, Odisha and the national capital territory of Delhi. He stressed that these could be the states where vaccination efforts could be concentrated; especially so in West Bengal, since this was the place from where the initial pandemics originated. However, he stressed the fact that introducing a vaccine was no child’s play; there were a number of hurdles to be crossed; some tough questions to be answered. This would ideally be done in a stop-wait-go mode, where if all the answers to the questions were “yes”, then one could “go” and introduce the vaccine; otherwise one would need to either “stop” or “wait”. Besides these, various policy issues related to vaccines with special reference to India were also discussed. Importantly, there was a big disjoint between the various ministries. Importantly, in India’s regulatory environment in the area of Biotechnology, there were many stakeholders, but unfortunately, no single ownership. He also talked about the Enteric diseases (Cholera, Typhoid and Polio) meeting held in New Delhi in April, 2013, in an effort to get all the stakeholders together. He finished off by talking about various advocacy issues, and by leaving a few questions for the audience, in particular, in what way could IDEA help in India’s efforts to introduce the vaccine. Dr. Hessel commented that this was a good introduction for the Policy and Advocacy workshops that were to follow on the coming two days.

Indonesia:

Indonesia’s presentation was entitled “Diarrhea in Indonesia” and was made by Dr. Mohammad Juffrie. The number of cases of outbreaks of diarrhea was studied between 2009 and 2013. There was a gradual decrease in the number of cases. The number of cases in 2009 was nearly 5000, which decreased to just over 3000 in 2010. In 2011, there was another peak at just over 4000 cases. The following year (2012), the number of cases dropped to ~1700. In 2013, the cases dropped even further to ~650. The corresponding deaths in the same years were also tabulated. The number of deaths was highest in 2009 at 110. It dropped to approximately 45 the following year (2010). In 2011 it dropped even further down to ~12 deaths. In 2012, there was a peaking to ~35 deaths. But in the following year (2013), there was a drastic fall to ~6 deaths. Therefore there was both a reduction in the number of cases as well as the number of deaths in 2013,

as compared to 2009. For the case fatality rate (CFR), the picture was slightly different. The CFR was highest for the year 2009, closely followed by 2012. The years, 2010 and 2013 were intermediate, while the year 2011 was the lowest.

From 3.30 PM to 3.45 PM there was a tea/coffee break. From 3.45 PM to 5.00 PM, the country presentations continued. In this session, there were to be four presentations, one each from Myanmar, Nepal, Pakistan and Sri Lanka.

Myanmar:

The Myanmar presentation was given by Dr. Htun Tin from the Ministry of Health, Myanmar. He began with the issue of emerging infections, and that our world was changing like never before. There was growth and movement of populations; rapid urbanization, coupled with a weak public health system. Importantly, in the current jet age, diseases travel much faster than before. He stressed on the adaptability of microbes due to changed circumstances; on antimicrobial resistance; on cross-over from one species to another, then to humans; as well as on global warming, environmental degradation, that is threatening international public health security. He then focused on cholera as a public health problem, indicating that it occurred primarily in areas with poor access to safe drinking water and adequate sanitation. He went on to highlight the other features of cholera, such as its ability to kill fast if rehydration is not instituted promptly; but with prompt and adequate treatment the CFR could be reduced to below 1%; the poor and marginalized populations at greatest risk of cholera often lack ready access to adequate health care facilities, and the use of oral rehydration therapy (ORT) for children with diarrhea is inadequate and declining in many cholera-affected countries. He talked at length about the various risk factors. He then went on to talk about communicable disease prevention and control. Talking about capacity building, he indicated that in Myanmar, there was a Field Epidemiology Training Programme, including the MPH programme at Yangon. He also indicated that an adequate pool of manpower was being developed in the various areas of the Health Sciences. After speaking about the WHO recommendation on cholera, he went on to indicate that the existing surveillance system was being evaluated and strengthened. He elaborated at length on how the surveillance system was being strengthened. He then went on to highlight the outbreak response policy of his country. He also discussed the preventive measures that were being adopted against cholera in Myanmar. In this context, he highlighted the role of the laboratory in cholera prevention and control. He also discussed the morbidity and mortality trend of diarrhea between 2006 and 2012. He concluded by sharing some of his experiences while working at the Ministry of Health in conjunction with cholera control.

Nepal:

Nepal's presentation was made by Dr. Shyam Raj Upreti, who is the Chief of the National Immunization Program at the Ministry of Health and Population, Nepal. His presentation was entitled "Cholera Control Update in Nepal". After giving a brief demographical introduction of his country, Dr. Upreti described the ecological regions, such as the Eastern Region, Central Region, Western Region, Mid-Western Region and the Far Western Region. He also described the

mountainous region, hilly region and the Terai region. Giving a brief introduction on the cholera situation in Nepal, he indicated that diarrheal disease, cholera in particular, was a major public health problem. Cholera is endemic in Nepal, with epidemic potential. In the Kathmandu Valley, cholera is an annual event during the rainy season. Frequent outbreaks also occur at various other places in the country. He indicated that the existing surveillance system was inadequate to cover all districts of the country. He added that the existing situation of water supply, sanitation and personal hygiene was favorable for cholera outbreaks. He highlighted the fact that surveillance for *V. cholerae* was integrated with antimicrobial resistance (AMR) surveillance, along with 8 other microbes. He added that surveillance included 18 participating labs spread out throughout the country. He described the distribution of *V. cholerae* isolates from the AMR network from 2006 till September 2013. Importantly, there has been a diminishing trend in recent years. He also described the distribution of the various serotypes of *V. cholerae* between 2006-2012. In most years, Ogawa was the predominant serotype. Here also, there was a general diminishing trend in recent years. The distribution of the *V. cholerae* isolates by age indicated that the age group of 15-30 years exhibited the highest isolation rates. There wasn't any appreciable difference in the gender distribution of the isolates. Monthwise distribution of cholera cases indicated that June – October was the cholera season in Nepal, with a peak in July. He then went on to highlight some recent cholera outbreaks in Nepal. He also indicated that there was a shifting of serotypes among *V. cholerae* strains in Nepal. Next, talking about prevention and control, he indicated that one of the major aims was to improve WaSH in the country, as well as the improvement of cholera outbreak response. He indicated that although cholera vaccination was not currently in the program, the NCIP had recommended its use along with other measures in the comprehensive cholera control package. In conclusion, although he suggested a way forward, he cautioned that there were issues also. He indicated that understanding the problem as a priority was still lacking, as there was no focused National Cholera Control Program; there was inadequate surveillance capacity, leading to under-reporting; in partnerships, the priority of the donors varied; efforts to improve WaSH in the short-term was not possible; a comprehensive and integrated approach to address the cholera problem was still weak; and finally, he also thought that the cost of the vaccine as well as financial sustainability were major issues.

Pakistan:

The Pakistan presentation was prepared jointly by Prof. Iqbal Memon and Prof. Mohammad Ashraf Sultan, but presented by the former. At the outset, Prof. Memon conveyed greetings from his country to the audience. He indicated that there was almost non-existing surveillance; proper reporting system was absent; there was a missing central link, as health was a provincial subject; moreover, sanitation and water supply was poor. He then went on to describe cholera between the years 2010-2013 with reference to alerts, outbreaks, total cases, confirmed cases and deaths. He also highlighted the geographical distribution of lab confirmed cases in the various provinces of Pakistan. The distribution pattern of the various serotypes and serogroups were also shown. He also presented the year wise comparison of suspected cases, confirmed cases, and

deaths under the disease early warning system (DEWS) of Pakistan; as well as the time and geographical distribution of the laboratory confirmed cases. The next set of statistics that he presented included pie charts representing the percentage distribution of cholera cases in the various provinces of Pakistan. The years covered were from 2010 to 2013. A cumulative data pie chart was also presented with data from August 2010 to 2013 end. Interestingly, from this chart, it is evident that the major provinces from where cholera cases were reported included Khyber Pakhtunkhwa (38%), Sindh (37%) and Punjab (12%). He concluded with a very touching and praiseworthy dedication to IDEA-Asia: Coming together – a beginning; Keeping together – progress; Working together – An achievement. This just about summed-up the 3 years of IDEA-Asia's existence. Everyone in the audience truly appreciated this quote.

Sri Lanka:

The Sri Lanka presentation was made by Dr. Paba Palihawadana, Chief Epidemiologist, Sri Lanka. The presentation was entitled "Diarrheal and Enteric Diseases in Sri Lanka". First she gave a brief overall introduction of Sri Lanka. She then indicated that the major water-borne diseases in Sri Lanka (2013) were viral hepatitis, dysentery and enteric fever. Importantly, there was no cholera in the country. This was followed by the incidence of the main water-borne diseases in Sri Lanka, which indicated that dysentery had the highest incidence, with the incidence of the other two diseases being far lower. She also indicated the incidence of viral hepatitis by month. With the exception for the year 2009, which peaked to 2000 in the month of June, the incidence in other years (2010-2013) was around 100-200. She also indicated the incidence of viral hepatitis for the year 2013, superimposed onto a map of Sri Lanka. She then went on to describe the incidence of dysentery by month. However, there was no clear pattern in the incidence, except for a peak in June for the year 2009. She also indicated the incidence of dysentery for the year 2013, superimposed onto a map of Sri Lanka. She then indicated the incidence of enteric fever over a period of 5 years (2009-2013). There were two clear peaks in June and September for the year 2009. Incidence (2013) was again represented superimposed on a map of Sri Lanka. Comparative maps of the three diseases were also presented for the year 2013. She also talked about the rotavirus surveillance, which has been ongoing since 2009 till date, and which has been funded by WHO. After briefly summarizing the rotavirus surveillance results, she went on to discuss about the outbreak control activities including chlorination and boiling of water prior to consumption. She went on to talk about water quality. She indicated that routine water quality surveillance was carried in Sri Lanka. Water samples were collected from all Medical Officers of Health (MOH) by Public Health Inspectors (PHI). Testing was carried out at the Medical Research Institute and the regional laboratories. She went on to present data on water quality for the years 2011-2013. Talking about sanitation, she indicated the availability of own toilets in urban, rural and estate areas. With regard to the disease surveillance machinery in Sri Lanka, she indicated that disease surveillance consisted of routine notification of communicable diseases; special surveillance on selected communicable diseases; and sentinel site surveillance. She then went on to talk about the notification system in Sri Lanka. Notification of communicable diseases is a legal requirement in Sri Lanka since 1897. Every medical practitioner or

person professing to treat diseases, who attends on any person suffering from any disease in the list would need to notify to the proper authority. Any person who contravenes this regulation would be guilty of an offence and such person can be prosecuted in a Magistrate Court. She then highlighted the list of notifiable diseases in Sri Lanka; as well as the mechanism of data collection. She finished off by highlighting a number of vaccines; namely typhoid vaccine (Vi polysaccharide vaccine), which was given to food handlers; the hepatitis A vaccine, which was not routinely administered; and the rotavirus vaccine, which was not in the EPI. The main question that was raised by this presentation was that how could the Sri Lankan government be so sure that cholera was absent in Sri Lanka?

DAY 2 (January 15, 2014)

The Meeting started at 9.00 AM with introductory remarks from the Ministry of Health, Government of the Philippines. The Ministry was represented by Dr. Theodoro Herbosa, Undersecretary of Health. Dr. Herbosa is a surgeon by training. He was a very jovial and down-to-Earth person. He spoke about his own experiences and the difficulties of delivering medical supplies during natural calamities, considering the rough and variant terrain of the Philippines. He indicated that sometimes one had to travel on horseback and sometimes even on foot. He also talked about his surgical years. He however indicated that he enjoyed his work, which was quite evident from his expressions. When he finished his speech, everyone applauded in appreciation for taking time out from his busy schedule to be with the IDEA group. He even stayed on till the beginning of the Advocacy Workshop.

Between 9.30 AM to 10.30 AM, an Introduction to the Advocacy Workshop was given by Dr. Luc Hessel and Dr. Sara Fröjdö. They reminded everyone of the basic aspects of advocacy. They also discussed about the various examples of successful advocacy initiatives, such as PATH, AREB, the rotavirus vaccine introduction initiatives etc. They then defined the objective of an advocacy document. Lastly, they presented the methodology for working sessions around three identified priorities viz. (i) Water and sanitation; (ii) Surveillance system and anticipation of events; and (iii) Vaccine introduction. Between 10.30 AM to 11.00 AM there was a pause for a photo session (Figure 1).

Insert Figure 1: "Participants at the 3rd IDEA Meeting"

The first session was primarily dedicated to "Concept and synopsis of advocacy document", which involved the designing of the advocacy document on three priority topics viz. (i) Targets, (ii) Content, and (iii) Format. In order to achieve these goals, the participants were divided into three subgroups so that each group could address each goal. The group activities were coordinated by a notekeeper (IDEA member) from each group, while the overall coordination was done by Drs. Luc Hessel, Sara Fröjdö and Marie Claude Bonnet.

Following lunch, the second session essentially concentrated on "Designing of the advocacy document". A review of the three groups was carried out with 20

minutes per group. This was followed by agreement on the synopsis by the three groups. The major outcomes were shared amongst the IDEA members by the notekeepers.

Further elaboration on the advocacy document was carried out during a third session. Besides the elaboration of the document, an implementation plan was developed for local, regional and national implementation. This was presented by each IDEA member notekeeper and overall supervised by Luc Hessel, Sara Fröjdö and Marie Claude Bonnet.

The Advocacy Workshop concluded with further final elaboration and fine-tuning of the advocacy document, as well as consolidation of the document and communication plan between all the IDEA members. The day's proceedings ended with sharing of all information between the various notekeepers, IDEA members and the coordinators. This ended with a first draft to be reviewed during the final session on Day 4 (Appendix 2).

DAY 3 (January 16, 2014)

The main highlight of Day 3 was a Policy Workshop. The Introduction to the Policy Workshop was given by Luc Hessel and Sara Fröjdö. This included general considerations on policy briefs including examples. These included objectives of policy brief, and presentation of methodology, for working sessions on identified priorities. This was followed by a brief presentation on the cholera calculator by Dr. Marie Claude Bonnet. The purpose of the Infectious Disease Cost Calculator (IDCC) developed by the UMPC Center for Health Security (<http://www.idcostcalc.org>) is to provide country-level disease cost estimates that can be used to inform decisions about investments in disease prevention and control at the local, national and global levels.

Then, the Policy Workshop focused primarily on the identification of policy goals. This was again done as in the Advocacy Workshop by splitting up into three groups. Each group was assigned a notekeeper from the IDEA members, while the overall supervision was done by Luc Hessel, Sara Fröjdö and Marie Claude Bonnet. The first focus was the consolidation of the policy goals. Presentations were made and reviewed in order to reach a consensus as to what to include in the policy document. Each presentation was 15 minute per group along with discussions. Following lunch, policy brief consolidation was carried out. Each group focused on 1-2 goals in terms of arguments to be considered for each policy goal; for example (i) What do we know? and (ii) What should we do? It was stressed that data needed to be collected in order to support these statements. These would either be available or had to be collected, or would have to be tailored for the purpose. Here also, the supervision was done in the same format as before. The last session of the day was dedicated to the consolidation of the document outline. (Appendix 3)

DAY 4 (January 17, 2014)

The topic for the final session (9.00 AM to 11.00 AM) was essentially “Alignment, Consensus and Conclusion”. The objective of the session was the review and validation of the Advocacy Material and Outline of the Policy Brief. The working plan for 2014 was also discussed with enthusiastic inputs from all the IDEA members. Dr. Hessel indicated that he would finalize the draft Advocacy Document and Policy Brief after taking inputs from the IDEA members. At the time of going to press, both the documents are complete and updated (Appendices 2 & 3). The meeting was a grand success and concluded with a vote of thanks by Dr. Luc Hessel.

References

1. Ali M, Sur D, You YA, Kanungo S, Sah B, Manna B, Puri M, Wierzba TF, Donner A, Nair GB, Bhattacharya SK, Dhingra MS, Deen JL, Lopez AL, Clemens J. Herd protection by a bivalent killed whole-cell oral cholera vaccine in the slums of Kolkata, India. *Clin Infect Dis* 2013; 56(8):1123–1131.
2. Bhattacharya SK, Sur D, Ali M, Kanungo S, You YA, Manna B, Sah B, Niyogi SK, Park JK, Sarkar B, Puri MK, Kim DR, Deen JL, Holmgren J, Carbis R, Dhingra MS, Donner A, Nair GB, Lopez AL, Wierzba TF, Clemens JD. 5 year efficacy of a bivalent killed whole-cell oral cholera vaccine in Kolkata, India: a cluster-randomised, double-blind, placebo-controlled trial. *Lancet Infect Dis* 2013; 13(12):1050-6.
3. Central Bureau of Health Intelligence (2012), Ministry of Health & Family Welfare, Govt. of India.
4. Ciglenecki I, Sakoba K, Luquero FJ, Heile M, Itama C, Mengel M, Grais RF, Verhoustraeten F, Legros D. Feasibility of mass vaccination campaign with oral cholera vaccines in response to an outbreak in Guinea. *PLoS Med* 2013; 10(9): e1001512.
5. Ivers LC, Teng JE, Lascher J, Raymond M, Weigel J, Victor N, Jerome JG, Hilaire IJ, Almazor CP, Ternier R, Cadet J, Francois J, Guillaume FD, Farmer PE. Use of oral cholera vaccine in Haiti: a rural demonstration project. *Am J Trop Med Hyg* 2013; 89(4): 617–624.
6. Kanungo S, Paisley A, Lopez AL, Bhattacharya M, Manna B, Kim DR, Han SH, Attridge S, Carbis R, Rao R, Holmgren J, Clemens JD, Sur D. Immune responses following one and two doses of the reformulated, bivalent, killed, whole-cell, oral cholera vaccine among adults and children in Kolkata, India: a randomized, placebo-controlled trial. *Vaccine* 2009; 27(49): 6887-6893.

7. Kanungo S, Sah BK, Lopez AL, Sung JS, Paisley AM, Sur D, Clemens JD, Nair GB. Cholera in India: an analysis of reports, 1997-2006. *Bull World Health Organ* 2010; 88(3): 185-91.
8. Longini IM Jr, Nizam A, Ali M, Yunus M, Shenvi N, Clemens JD. Controlling endemic cholera with oral vaccines. *PLoS Med* 2007 Nov 27; 4(11): e336.
9. Luquero FJ, Grout L, Ciglencecki I, Sakoba K, Traore B, Heile M, Dialo AA, Itama C, Serafini M, Legros D, Grais RF. First outbreak response using an oral cholera vaccine in Africa: vaccine coverage, acceptability and surveillance of adverse events, Guinea, 2012. *PLoS Negl Trop Dis* 2013; 7(10): e2465.
10. Rouzier V, Severe K, Juste MA, Peck M, Perodin C, Severe P, Deschamps MM, Verdier RI, Prince S, Francois J, Cadet JR, Guillaume FD, Wright PF, Pape JW. Cholera vaccination in urban Haiti. *Am J Trop Med Hyg* 2013; 89(4): 671-681.

APPENDICES

Appendix 1: Agenda

Appendix 2: Advocacy document

Appendix 3: Policy Brief