Introduction of New Vaccines

Report of a Regional Consultation
Bangkok, Thailand, 11–13 December 2012

World Health Organization
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Annexes

Acronyms

BCG	bacillus calmette–guérin (vaccine)
bOPV	bivalent oral polio vaccine
DTP	diphtheria-tetanus-pertusis vaccine
EPI	Expanded Programme on Immunization
FDA	Food and Drug Authority
GAVI	Global Alliance for Vaccines and Immunization
GDP	gross domestic product
GIVS	Global Immunization Vision and Strategy
GVAP	Global Vaccine Action Plan
Hib	Haemophilus influenzae type b
HITAP	Health Intervention and Technology Assessment Programme
HPV	Human papilloma virus
HSS	health system strengthening
HTA	health technology assessment
ICC	Interagency Coordination Committee
IEC	information education and communication
IRI	intensification of routine immunization
IHPP	International Health Policy Programme
IPD	invasive pneumococcal diseases
IPV	inactivated poliomyelitis vaccine
JE	Japanese encephalitis
JRF	Joint Reporting Form (WHO–UNICEF)
MDG	Millennium Development Goals
MIC	Middle-income country

MLM	mid-level management
MR	measles and rubella
NCIP	National Committee for Immunization Practices
NHSO	National Health Security Office
NIP	national immunization programme
NITAG	National Immunization Technical Advisory Group
NLEM	national list of essential medicines
NRA	national regulatory authority
NUV	new and underutilized vaccine
NUVI	new and underutilized vaccine introduction
NVC	National Vaccine Committee, Thailand
OCV	oral cholera vaccines
OPV	oral polio vaccine
PATH	Programme for Appropriate Technology for Health
PHC	primary health care
PCV	pneumococcal conjugate vaccine
PMS	post-marketing surveillance
QAC	Quality Assurance Centre
QALY	quality-adjusted life years
SAGE	Strategic Advisory Group of Experts on Immunization
SEAR	South-East Asia Region
SIA	supplementary immunization activities
SIVAC	Supporting Independent Immunization and Vaccine Advisory Committees
tOPV	trivalent oral polio vaccine
VIS	vaccine investment strategy
VPD	vaccine preventable disease

1. Background and objectives

The national immunization programmes (NIP) of all Member States of the South-East Asia Region of WHO have had BCG, OPV, DTP, and measles vaccines since 1970s. With the inception of expanded programme of immunization globally, several Member States have introduced additional vaccines in their NIPs in recent years.

All Member States in the South-East Asia Region (SEAR) have introduced Hepatitis B vaccine. Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Myanmar, Nepal, Sri Lanka and Timor-Leste have introduced the *Haemophilus Influenzae* type b (Hib) vaccine with financial support from the Global Alliance for Vaccines and Immunization [GAVI]. In addition, Member States those are endemic for Japanese Encephalitis (JE), such as India, Nepal, Sri Lanka, and Thailand, have introduced JE vaccine in the high risk districts. Out of these, Sri Lanka and Thailand have now expanded JE vaccination to all the districts in their countries.

Rubella vaccine has been introduced as Mumps Measles Rubella (MMR) vaccine in Maldives, Sri Lanka and Thailand and as Measles and Rubella (MR) vaccine in Bangladesh and Bhutan. Additionally, Bhutan has introduced the human papilloma virus (HPV) vaccine. Two pilot/demonstration projects are on for rotavirus vaccine and for IPV in Thailand and Indonesia respectively. Apart from these, there are many more new vaccines that are already available, or will soon be available in the market, that have potential to be introduced during the next 10–15 years.

A regional meeting on vaccine prioritization was conducted in May 2009 and new and underutilized vaccines (NUV) were prioritized into three groups for introduction in the immediate future (3–5 years), for near future (5–10 years) and for the distant future (in 10 years). In addition, a set of criteria were identified for prioritizing a new or underutilized vaccine for introduction in a national programme.

However, with the availability of a plethora of vaccines and the changes in the vaccine market following the introduction of newer vaccines by more countries, the countries of the Region have begun to feel the need for a more focused approach and a better-defined strategic framework to support the decision-making process in inclusion of new and underutilized vaccines in their respective NIPs. This need was expressed in many high-level regional meetings held during the last two years. This became very much a felt need following the realization that there was a global shortage of DTP vaccine as a result of more countries introducing Hib containing pentavalent vaccine in their NIPs.

The current regional consultation on introduction of new vaccines was conducted to review the criteria that were identified in the 2009 meeting and develop a decision-making algorithm for new and underutilized vaccine introduction (NUVI) for the Region. The consultation brought together the key technical experts and EPI managers from Member States for this purpose and reviewed the existing criteria and agreed upon a draft decision-making algorithm for countries to use at the national level in introducing NUV in the future.

The general objective of the Regional Consultation was to agree on a regional framework for introduction of new vaccines in the SEA Region that will enable Member States to make rational decisions on new and underutilized vaccine introduction.

The specific objectives of the Regional Consultation were as follows:

(1) To review the country progress and status in introducing new vaccines since the year 2000;

(2) To review lessons and challenges faced by countries in the last 12 years;

(3) To review the existing framework for introduction of new vaccines in the SEA Region;

(4) To identify and agree on a set of criteria to be fulfilled by each country depending on its present achievements and the capacity while introducing new vaccines.

The Regional Director, Dr Samlee Plianbangchang, inaugurated the consultation. The Regional Director's opening remarks are available in

Annex 1. Dr Syed Abu Jafar Md. Musa, Ministry of Health and Family Welfare, Bangladesh, chaired the meeting, while Dr Aishath Thimna Latheef, Public Health Programme Manager, Centre for Community Health and Disease Control, Ministry of Health, Maldives, acted as the Rapporteur.

Participants from 10 out of 11 Member States representing their national programmes of immunization attended the consultation. The agenda and list of participants are available in Annex 2 and 3 respectively.

2. Proceedings

2.1 Implementation of "2012: Year of Intensification of Routine Immunization"

At the outset, a brief update on "implementation of "2012: Year of Intensification of Routine Immunization (IRI)" was provided including the status and magnitude of the cohort of unimmunized children in the SEA Region. India, Indonesia and Timor-Leste were pointed out as priority countries for intensified attention in the Region. Among estimates of the percentage of children missing DTP3 in the Region, 85.6%, 8.7%, 2.2% and 1.8% were from India, Indonesia, Bangladesh and Myanmar respectively. The estimated number of missing children for DTP3 in the Region was 8.7 million. As far as the district coverage for DTP3 below 80% was concerned, several countries still had to achieve the target.

The objective of 2012-Year of Intensification of Routine Immunization included achieving Global Immunization Vision and Strategy (GIVS) Goal of a minimum coverage of third dose of DTP containing vaccines 90% at national and 80% at sub-national levels. All Member States had prepared and started implementing country-specific plans for Intensification of immunization focusing on increased access on hard-to-reach, underserved, marginalized and migrant populations. Several Member states launched IRI with high level participation. All countries approached the implementation of IRI with innovative ideas such as branding immunization with new logos, IEC materials, emphasizing mid-level management (MLM) training, mobilizing communities to reach targeted children, filling vacancies of vaccinators/PHC workers and providing flexible immunization schedules.

Highlighted issues and challenges faced in IRI included delays in implementation, limited or non-availability of additional funding, inadequate human resources, non-availability of vaccines, inadequate implementation of monitoring and supervision plans, not focusing on priority districts but addressing common issues in some Member States that will have limited direct effect on increasing coverage, not sharing data in a timely manner, and, inaccurate denominators/coverage mostly at sub-national levels.

The recommendations made in the EPI review meeting held in October 2012 were development of monitoring tools, strengthening of surveillance to measure impact, development of user-friendly Standard Operative Procedures for reaching the unreached, building the 2012 Year of Intensification into a multiyear intensification plan along with GVAP and using GAVI HSS funds where applicable, to strengthen health systems for gaining immunization outcomes.

It was suggested that the impact of IRI be reviewed by means of selected immunization cluster surveys, EPI review meeting in June/July 2013, Regional Committee meeting in September 2013 and the final review of "2012 Year of intensification of RI" in February 2014 along with regional certification of polio eradication. It was pointed out that IRI will protect the polio-free status, facilitate maternal and neonatal tetanus elimination, set the stage for measles elimination and rubella/CRS control and improve programme capacity for introduction of additional antigens. Additionally, IRI will improve awareness on immunization even at the highest level with advocacy, enhance system strengthening for immunization delivery, increase access, coverage, strengthen surveillance and improve monitoring and supervision.

Discussion points

- The Sixty-fifth World Health Assembly adopted Resolution WHA65.18 "World Immunization Week" in May 2012; it could be used as one of the strategies for IRI.
- The RI monitoring tool may be highlighted for developing better understanding among country programme managers.

- Surveillance function of national EPI teams needs to be strengthened to overcome their limited capacity to conduct VPD surveillance;
- In counteracting the anti-vaccine lobbying, Member States should improve the capacity of vaccine quality monitoring; develop national capacity for communicating risk of AEFI (Risk communication plan): There should be a pro-vaccine lobbying mechanism targeting the general public to promote vaccine as a broader disease control measure.

2.2 Regional decision-making framework for NUVI

The NUVI decision-making experience in the Region in the context of current immunization systems was outlined and the next steps highlighted. Participants were briefed about the availability of many new vaccines and of those in the pipeline, the immunization goals and targets set for 2015, MDG4, the regional targets, the "Year of Intensification of Immunization", the funding availability from many new initiatives, the need for achieving immunization outcomes for GAVI's health system strengthening (HSS) support, the interested parties, advocacy groups and the need for protecting the current level of support for immunization beyond 2015.

It was necessary to determine whether national immunization programmes should wait for strengthening programme capacity prior to introducing a new vaccine or use the opportunity that comes along with the NUVI for training, improving cold chain system and logistics, developing information education and communication efforts, and strengthening surveillance, monitoring and evaluation of the existing programme. The different stakeholders and processes influencing the national EPI decision-making pathways for NUVI, such as the external interested groups, national immunization technical advisory groups, the Strategic Advisory Group (SAGE) recommendations, international goals (MDG4) and targets, disease burden, affordability, acceptability, cost-effectiveness and cost benefit analysis were explained.

Challenges posed by the anti-vaccine lobbying groups, the need to complete phased introductions, Member States graduating from GAVI support, sustainability, continuing reliance on external support for proposal and report writing, accountability at different levels were highlighted.

Thereafter, the objectives of the 2009 "Vaccine prioritization workshop", agreed criteria, the "immediate" priority list, "near future" priority list and the "distant" priority list along with the status of different vaccines available globally and regionally were clarified and the next steps expected to be achieved by the consultation described. Participants were sensitized on the importance of concentrating on six vaccines (human papillomavirus vaccine (HPV), pneumococcal conjugate vaccine (PCV), rotavirus vaccine, typhoid vaccine, cholera vaccine and the inactivated polio vaccines (IPV), out of which cholera and typhoid were the regionally important vaccines.

2.3 Achieving MDG4: potential contribution of new and underutilized vaccines

Although there had been a 41% reduction in global under-five deaths from 12 million in 1990 to 6.9 million in 2011, it was unlikely that the world would achieve the MDG4 target of two-third reduction of child mortality by 2015, since 75% of child deaths were due to neonatal causes, pneumonia, diarrhoea, malaria, measles and HIV/AIDS. The WHO strategies in response to this challenge were appropriate home care and treatment of complications for newborns; integrated management of childhood illness; Expanded Programme on Immunization; infant and young child feeding and skilled care during pregnancy and child birth.

While there was the unfinished task of controlling the traditional vaccine preventable diseases such as polio, diphtheria, pertussis, tetanus, and measles, there were opportunities to achieve success in controlling other VPDs i.e. those caused by JE, rubella, influenza, yellow fever, hepatitis B, Hib, typhoid, cholera, pneumococcus, rotavirus, HPV and epidemic meningitis. Further vaccines against TB, malaria, dengue and HIV/AIDS were in the pipeline and it was hoped that a dengue and malaria vaccine might become available for use after 2015.

The main causes of vaccine-preventable deaths in children under five in the year 2008 were pneumococcal diseases (32%), rotavirus diarrhoea (30%), Hib (13%) and pertussis (13%), measles (8%) and tetanus (4%). The estimated global burden for pneumococcal disease in children under five years of age in 2008 was 14.5 million cases and 541 000 deaths. The highest pneumococcal mortality rates were seen in South Asia and Africa.

Three pneumococcal conjugate vaccines were available for use – PCV7 (now being phased out), PCV10 and PCV13 with slightly different serotype coverage and differing cold chain volume. The issue of serotype replacement following PCV introduction was recently discussed by the WHO Strategic Advisory Group of Experts on Immunization which saw a reduction in PCV 7 serotypes in < 5 year and > 5 year olds in all populations with an increase in non-PCV7 serotypes in both age groups. However, there was a reduction in overall invasive pneumococcal diseases (IPD) and meningitis in < 5 year population while the impact on overall IPD in older age group was variable. It was also reassuring to note that the replacing serotypes were mostly present in PCV10 and PCV13. SAGE thus concluded that no changes were required in PCV recommendations, but that there was a need for continued monitoring for *Streptococcus pneumoniae* serotype replacement.

The positive impact of PCV in reducing IPD in the USA and several other settings was stressed and very recent reductions of hospital IPD admissions in Kilifi, Kenya were illustrated. More than 80 countries have to date introduced pneumococcal conjugate vaccines, many with support from the GAVI Alliance. Several new pneumoccal vaccine candidates were under development, including protein vaccines in early clinical stages.

Rotavirus was the most common cause of severe dehydrating diarrhoea among children worldwide and in 2008, caused more than 100 million cases, 25 million outpatient visits, 2 million hospitalizations and more than 450 000 child deaths. Global surveillance showed that around 40% of diarrhoeal hospitalizations were on account of rotavirus. Preventing serious disease due to rotavirus was the best way to protect children in low-income countries, as improvements in sanitation and hygiene that stop many bacteria and parasites did not prevent the transmission of rotavirus, and children in developing countries were not getting the maximum benefits from life-saving treatment options. Rotavirus mortality was the highest in South Asia and Africa. Two WHO pre-qualified rotavirus vaccines were currently available (a monovalent human and a pentavalent bovine-human vaccine with high efficacy against the severe rotavirus gastroenteritis caused by prevalent rotavirus strains). Vaccine impact correlated inversely with disease incidence and WHO child mortality strata, possibly due to competing enteric viruses, maternal antibodies (trans-placental, breast milk), age at time of first dose, interval between doses, concurrent oral

polio vaccines use, malnutrition or normal gut flora differences in high- and low-income settings. Overall, however, the burden of disease prevented appeared to be greater in low-income settings due to the higher incidence of severe rotavirus gastroenteritis in the latter.

Vaccine impact in low mortality settings was clearly demonstrated by six independent US hospital-based studies reporting a 85 - 95% reduction in rotavirus cases in 2008 after vaccine introduction. Also in Australia, diarrhoea hospitalizations were drastically reduced after use of rotavirus vaccines. In Mexico and Brazil, on the other hand, a 35% and 22% reduction in overall diarrhoea-related mortality was observed in children under five years following the introduction of rotavirus vaccines.

Rotavirus vaccines were now in use in the national inmmunization programmes in more than 40 countries, partly supported by the GAVI Alliance. A number of new rotavirus vaccines from Indian and Indonesian manufacturers were presently undergoing phase II and phase II clinical trials.

Regarding human papilloma virus (HPV) disease, it was stated that cervical cancer was responsible for 275 000 deaths worldwide in 2008, among them 159 000 in Asia. In 2008 alone, 529 000 new cases were reported and that South-Central Asia was considered a high-risk region with cervical cancer remaining the most common cancer in women there. It was expected that introduction of HPV vaccination would exert an impact on the attainment of the MDGs, through avoidance of orphaned children and families whose mothers died or were disabled due to cervical cancer (MDG1; keeping women healthy so they would not die young, reduction of disproportionate female burden linked to reproduction (MDG3); strengthening of comprehensive reproductive health services (MDG5); reduction of HPV infection which may in turn reduce HIV infections (MDG6) and finally, through enhancing partnerships with noncommunicable disease, cancer control, reproductive, adolescent and school health and HIV patients and service providers (MDG8).

Two HPV vaccines were widely licensed and WHO prequalified a bivalent vaccine against HPV types 16 and 18 and a quadrivalent vaccine against HPV types 16/18 as well as HPV types 6 and 11 with excellent safety profiles and to best be administered to HPV naive individuals before

onset of sexual activity. The present WHO position was that HPV vaccination should be introduced into national immunization programmes where prevention of cervical cancer was a public health priority and where vaccine introduction was programmatically feasible and financially sustainable. Use of the vaccine could potentially reduce the lifetime risk of cervical cancer by up to 50%. Challenges to vaccine introduction were the present vaccine costs (now reduced substantially for GAVI procurement), and the relatively high vaccine delivery costs in developing countries due to the fact that new delivery approaches were needed. On the other hand, HPV vaccination provided unique opportunities to bring new energy and advocacy to interdisciplinary coordination and to establish strong partnerships with stakeholders in reproductive health, adolescent health, school heath, cancer control and women's health.

Typhoid fever was an often ill-recognized public health problem with an estimated 21 million cases annually resulting in more than 200 000 deaths that affected predominantly school children but in some endemic areas also children below five years of age. Ninety percent of deaths from typhoid were in Asia where rising drug resistance made treatment more difficult. The typhoid disease burden was substantiated by several recent studies including a cost-of-illness study which revealed that the average private cost of a non-hospitalized case was 13% of an average monthly household income in Kolkata, India (US$ 84), 23% in North Jakarta, Indonesia (US$ 207) and 55% in Hechi China (US$ 121). The cost of a hospitalized case was 35% of income in Kolkata and over 100% in North Jakarta and Hechi. Two typhoid vaccines were presently in use the Vi-polysaccharide injectable vaccine and the TY21a live oral vaccine, both not recommended for children below the age of two years and with limited duration of protection. Several conjugate vaccines were in different development stages out of which at least three were in India and the GAVI Alliance had decided to support introduction of such new conjugate vaccines, after WHO prequalification.

According to WHO estimates, more than 3 million cases and 100 000 – 130 000 cholera deaths occurred annually, with more virulent variants and antibiotic resistant strains emerging. Cholera was now endemic in about 50 countries affecting mostly young children, and epidemics had been recently occurring in Haiti, Pakistan, Papua New Guinea, Philippines, Sierra Leone and Zimbabwe with often severe negative economic impact.

Two WHO prequalified oral cholera vaccines were available and six more were in the developmental stage, with one producer of a pipeline vaccine in India in the clinical trial phase. The WHO position paper on cholera vaccine was updated in 2010. Improvements to low-cost supply of these vaccines were needed and work needed to proceed on developing single-dose vaccines not requiring clean water for administration.

There were mixed expectations for the dengue, malaria, HIV and TB vaccines to be available for use in the near future, with *p. falciparum* malaria vaccine not being available before 2016 at the earliest. There was a need to review further results of dengue vaccine clinical trials before being able to make predictions on the availability of a dengue vaccine for use in national programmes.

The challenges faced by the developing countries in introducing new vaccines e.g. uncertainty about the disease burden, weaknesses of immunization systems, financial sustainability and fears or misinformation about new vaccines were also discussed. In addition to their potential for reducing the disease burden of Hib, pneumococcal and rotavirus disease, introduction of these vaccines will provide opportunities for assessment of vaccine impact through improved surveillance and data collection and for generation of demand through increased publicity and media attention. The health work force will receive training and supervision during the vaccine introduction. Apart from these, new vaccines introduction helps in the development of more appropriate vaccine formulations and presentations globally and increases attention to supply and cold chain management issues. Moreover, new financing mechanisms have been introduced globally to support the introduction of new and underutilized vaccines; such as the advance market commitment and the international finance facility for immunization. Also, along with this process, countries have allocated more domestic resources for immunization. Last but not the least, new vaccine introduction has created new opportunities to strengthen leadership and governance including regulatory policy frameworks and improved accountability procedures with spillover effects to other health programmes.

2.4 New and Underutilized Vaccines Introduction (NUVI) in SEAR

The status of new and underutilized vaccines introduction (NUVI), NUVI and DTP3 coverage, factors influencing the decision-making process, diseases under consideration, opportunities for strengthening RI and challenges for NUVI in the SEA Region were elaborated.

Of NUVIs in the Region, live Japanese encephalitis vaccine SA-14-14-2 is used in 112 of 644 districts in India, 27 of 75 districts in Nepal and all districts in Sri Lanka, while inactivated JE vaccine is used in all districts in Thailand. The birth dose of hepatitis B is given in Bhutan, Democratic People's Republic of Korea, India, Indonesia, Myanmar, Maldives and Thailand. A higher coverage of birth dose of Hepatitis B has been achieved in Democratic People's Republic of Korea, Indonesia, Maldives and Thailand. Hepatitis B vaccine in the form of tetravalent vaccine is given in Indonesia and Thailand and in the form of pentavalent (DTP, Hepatitis B and Haemophilus Influenza type B [Hib]) in Bangladesh, Bhutan, Democratic People's Republic of Korea, India (08 States), Maldives, Myanmar Nepal, Sri Lanka and Timor-Leste. Rubella vaccine is given in the form of MMR in Maldives, Sri Lanka, and Thailand and as MR in Bangladesh and Bhutan. HPV vaccine is given in Bhutan. How Member States introduced different new vaccines with the consolidation of DPT3 coverage was highlighted.

Among 25 NUVI events across seven countries responded to an IVD inquiry on the factors that influenced decision-making during the past. It was revealed that in 23 events, the national EPI team recognized the need and discussed at the NCIP (NITAG). Other factors influencing NUVI included increased disease burden in 8 events and specific research evidence in 7 events, internal influence in 12 events, as the next step in EPI for continuation of basic antigens in 15 events, Government recognition of the need and fully financed in 12 events and direct external support in 13 events.

Current global use of NUV and diseases under consideration for NUVI in the Region was discussed in terms of number of countries using, GAVI eligible status, use in other regions. Of these diseases under consideration for NUVI in the SEA Region, seven rotavirus surveillance and six invasive

bacterial disease surveillance sentinel sites were functioning including a field site in Bangladesh. The other countries having sentinel sites are Indonesia, Myanmar, Nepal and Sri Lanka. The two regional referral laboratories are in India. Though numbers were small, these sites were generating important evidence related to rotavirus strains, pneumocoocal serotypes, haemophillus influenza and neisseria meningitides in the SEA Region. Surveillance data of 2011 and 2012 were shared with participants. For HPV, available incidence and mortality of cervical cancer in the SEA Region was presented.

Strengthening the functions of the national technical advisory groups on immunization (NITAGs), national regulatory authorities (NRAs) on vaccines, reaching the unreached children and supporting human resource development contribute to strengthening routine immunization through NUVI. In addition, improvements in overall management of expanded programme on immunization (EPI) and its capacity by addressing issues related to cold chain capacity, injection safety, strengthening surveillance of vaccine preventable diseases and adverse events following immunization, exploring the possibilities of procuring vaccines through joint procuring mechanisms also contribute to strengthening routine immunization through NUVI.

The challenges for NUVI in the SEA Region were strengthening NCIP/NTAGIs for countries, making evidence-based decisioning, decreasing dependency of countries on donor support, introducing innovative mechanisms to reduce high cost of new vaccines and addressing the issue of financial sustainability, ensuring achievement and maintaining high coverage, committing to co-financing payment plans, continuing surveillance with laboratory support, counter-acting allegations made by the anti–vaccine lobbying groups, and monitoring and responding to AEFI.

2.5 Implementation of new and underutilized vaccine global experience

The principles for adding a new vaccine into an existing immunization system were highlighted as having a strong decision-making process; a well performing or improving (based on past performance) immunization programme as an integral component of comprehensive health promotion

and disease control and prevention efforts with sufficient human and financial resources and guaranteed vaccine supply.

Already 179 of 193 Member States (93%) had introduced Hib containing vaccine globally and in 2012 the GAVI Alliance had received eight more new applications. While more than a quarter of the world's children still do not have access to Hib vaccine, recent developments such as India having introduced it in several states since 2011, Russia having introduced partially in 2011, Nigeria in 12 states since 2012 and Indonesia planning to introduce in four provinces in 2013 will further improve global Hib coverage.

With regard to pneumococcal conjugate vaccine (PCV), it was reported that within 1.5 years after first introduction in developed countries, PCV was introduced in a developing country and altogether it was in use now in 80 countries (of which 26 low or low-middle income). An opportunity was available for GAVI graduating countries to apply for a dose price of US$ 3.50, through the advance market commitment mechanism. Some of the challenges of PCV introduction were; constrained vaccine supply in 2012 and 2013 to cater to the demand, need to closely monitor pneumococcal serotypes, as well as comply with stringent conditions related to the PCV10 2-dose vial presentation without preservative.

Rotavirus vaccines are now in use in 40 countries. Recent active post-marketing safety surveillance in Mexico and Australia detected a small increase in the risk of intussusception shortly after the first dose of rotavirus vaccines, a risk which was not documented in the US to date, and based on this information, WHO SAGE noted that benefits documented with rotavirus vaccine outweighed the risk of vaccine-associated intussusception and that countries could remove the present age restrictions (first dose before 15 weeks of age and last dose before 32 weeks of age) based on a risk-benefit analysis. This means that countries are to strengthen post-marketing safety surveillance and review the timeliness of DTP/penta and rotavirus vaccine administration; the peak age of rotavirus gastroenteritis cases and deaths; and estimate potential additional intussusception deaths as well as prevented rotavirus deaths when choosing a schedule without age-limitation. Health staff will need to be informed of the small potential risk of intussusception after rotavirus vaccination and to ensure caregivers

are adequately counselled to recognize early signs of intussusception, and encouraged to present cases immediately for medical attention.

Forty one countries have to date introduced human papilloma virus (HPV) vaccine in their national programmes and 15 countries have applied for HPV vaccine demonstration projects. The GAVI Alliance has increased its support for operational cost for HPV vaccine introduction to 2.40 US$/targeted girl. HPV vaccination should be implemented as part of a comprehensive approach to cervical cancer control and WHO has developed a cervical cancer prevention and control costing tool as well as vaccine coverage monitoring tools, which are available to countries. Challenges with HPV vaccination related to reaching the target population of 9–13 year old girls in or outside schools; increased collaboration needs on cervical cancer prevention, screening and treatment; and adjunct adolescent health and cancer control interventions.

WHO has recommended typhoid vaccines for outbreak control, starting vaccination in the early stages of an outbreak, as well as for controlling endemic disease through vaccination on high-risk population groups, and to strengthen typhoid surveillance. There is a need to implement a comprehensive multidisciplinary approach including safe water and sanitation, early diagnosis and prompt treatment with appropriate antibiotics. The GAVI Alliance will open a support window for typhoid vaccines only after availability and WHO prequalification of a conjugate vaccine.

Two oral 2-dose cholera vaccines are now WHO prequalified with similar performance. WHO's recommendation for use of cholera vaccination is a risk-based approach, in endemic and high risk areas or groups or populations in conjunction with other prevention and control strategies (e.g. improving water and sanitation). Pre-emptive vaccination may prevent outbreaks or the spread of current outbreaks and predictive risk-assessment will help decision-making on the need for such vaccination. Reactive vaccination may be an additional control measure, depending on local infrastructure and the epidemiological situation. The mainstay of control during epidemics should be appropriate treatment of cholera patients along with other preventive measures.

Discussion points

- The global experience of using 2-dose and 3-dose rotavirus vaccines in relation to identifying optimal schedule, impact of 10-valent pneumococcal vaccines on non-typeble *Haemophilus influenza*, and consent of adolescent girls for HPV vaccination was shared. The South-East Asia Region should adopt integrated disease control approaches for the control and prevention of VPD (cervical cancer, diarrhoeal diseases, pneumonia and acute respiratory infections).
- Vaccines that have a proven herd effect (e.g. rotavirus, pneumococcal) need fast track introductions: an advocacy plan is to be developed.
- The contribution of new vaccine use to overall economic development is to be highlighted.
- Focusing only on increasing vaccine demand to improve affordability of the new vaccines is not adequate; the global community should negotiate with manufacturers for a reduction of the vaccine prices; it will be important to enlist the proactive engagement of economists at all levels of these discussions.
- The South-East Asia Region should consider a strategy for the elimination of typhoid fever as a regional priority; a request should be made for developing typhoid vaccines including vaccines against paratyphoid.
- Cholera vaccines could be used in response to outbreaks.

2.6 Update of Japanese encephalitis/acute encephalitis syndrome (JE/AES) in the South- East Asia Region

An update of Japanese encephalitis/acute encephalitis syndrome (JE/AES) in the South-East Asia Region, was provided. JE is the commonest cause of encephalitis worldwide. Fifty thousand cases and 15 000 deaths are reported every year across Asia mostly in children. Fifty percent of survivors have neurologic sequalae. In the South-East Asia Region, India, Nepal, Sri Lanka and Thailand have introduced vaccines and JE/AES surveillance is in place while Bhutan, Bangladesh, Indonesia, Myanmar and Timor-Leste have only JE/AES surveillance. The Regional Office collects monthly JE/AES

surveillance data and includes the surveillance data in the VPD surveillance report. The Region has one reference laboratory and 13 national laboratories out of which seven are in India. Democratic People's Republic of Korea and the Maldives do not have national laboratories and both countries are yet to introduce JE/ AES surveillance. In Nepal, Sri Lanka and Thailand, the proportion of JE among AES has dramatically decreased over the years following successful vaccination. However, in all countries, still AES cases are being reported and the aetiology is not fully understood. In India, outbreaks do occur in areas where JE vaccination has been introduced and immunization status of the cases is not fully understood. Continuation of vaccination for new cohorts, introduction of catch-up campaigns when necessary, expansion of vaccination to remaining high risk areas, expansion of laboratory-based surveillance are challenges to be addressed.

The multi-country JE project by Programme for Appropriate Technology for Health (PATH) succeeds the previous JE projects that were in existence from 2004–2011 and the mission is to eliminate clinical JE and avoid unnecessary deaths and disability due to this disease. There were five vaccine candidates on trials and at least three were expected to be WHO-prequalified by end 2013. Ten countries had registered SA-14-14-2 vaccine in Asia. The duration for the present multi-country JE project would be for five years up to 2017 and it has planned to support six countries of the Region for supporting introducing vaccines and sharing experiences. The project will identify regional training centres and facilitate training, support sharing of information by enabling bi-regional meetings and develop a web-based JE data base. Among other activities, it includes to provision of technical assistance, development of prototype surveillance, standard protocols and guidelines and facilitation of uninterrupted vaccine supply.

Discussion points

- JE impact in the South-East Asia Region should be documented: PATH-JE Project can help in publishing JE experiences; ecological studies to measure true impact & CEA; burden of AES and JE including associated disability and productivity gain by preventing disabilities need to be researched and documented.

- An evaluation of acute encephalitic syndrome surveillance should be carried out and linking it with meningitis surveillance needs to be explored.

2.7 Health systems strengthening: issues and challenges for new and underutilized vaccine introduction (NUVI)

Frequent and sometimes large changes in DTP3 coverage were no longer likely to occur following NUVI than in non-introduction years. Also, no association between new vaccine introduction and changes in DTP3 coverage had been found in models. Service delivery wise, NUVI enabled mobilization of people, increased through enhanced publicity and media attention, better training, supervision of the health work force, improving data collection, data reporting and enhanced surveillance. Vaccines and technologies had introduced more appropriate formulations and presentations for low-income countries, improved vaccine management results in reduced wastage, provided more precise forecasts to prevent stock-outs or over-stocking at the national level, focused more attention to cold chain management, assessed and refurbished the cold chain and evaluated controlled temperature chain use. Strengthened regulatory policy frameworks, national immunization technical advisory groups, national regulatory authorities, improved accountability procedures, increased efforts to engage parliamentarians and civil society and the spillover effect to other health programmes had contributed immensely to good governance and leadership. NUVI had also added a new dimension to coordinated and comprehensive approaches to pneumonia and diarrhoea prevention and treatment and cervical cancer control strategies.

Identifying health systems gaps in improving the output and outcome of the programme was important. The gaps may be identified from recent assessments that may have been carried out, drawing national plans and strategies, surveys and existing reports, and consultations. Key systems, operational and management issues and barriers in terms of community and household level, health services delivery level, health sector policy and sector management level were presented. The need for detailed consideration of health systems building blocks was stressed. Health system strengthening involved improving the six building blocks and managing interactions between them in ways that achieve more equitable and sustained improvements across services and health outcomes.

Common constraints, gaps and challenges in health systems were observed in areas such as availability, skills, motivation of health workers, supplies, procurement, distribution systems, cold chain, laboratory services, access in particular financial access, management and coordination of services , information and monitoring systems.

Strengthening service delivery and infrastructure included improving Infrastructure and services in rural, urban, private and other sectors, logistics such as cold chain, supplies, access, coverage, privacy respect, and dignity and client satisfaction. Improving health information systems surveillance and reporting required focus on adverse events-related operational problems, research to generate evidence for policies, monitoring of implementation, evaluation and capacity development related to technology. Strengthening human resources required ensuring adequate numbers and the right mix, attitudes and behaviour, career development, training and retraining. The financing aspects that needed attention for strengthening were determining the costs of services, recovering fee for service, donors of funds, shifting of funding sources and the challenge of ensuring sustainability of financing.

2.8 New vaccine introduction for public health benefits in Thailand

Health intervention and technology assessment (HITAP) was the research arm of the Bureau of Health Policy and Strategy, Ministry of Public Health that appraised a wide range of health interventions and technologies including health promotion and public policy in Thailand.

In the case of HPV infection, it is the second most common cancer with more than 8 000 Thai women diagnosed each year. The coverage of screening (20%) was poor, though the screening was offered to all women between 35 and 60 years of age since 2002. WHO, GAVI and IVI had carried out several activities to facilitate the use of HPV vaccine in Thailand. Two HPV vaccine products had been approved by the Thai FDA in 2007 with strong direct and indirect public communication about the vaccine. Thus, it had gained political attention in Thailand.

However, there are differences between HPV vaccine and other vaccines. Unlike other vaccines that take less than 20 years to produce full

effects, HPV vaccination would take 30–40 years. HPV vaccine is unlikely to have externalities. It is a teenager's vaccine delivery of which is challenging. As compared to other vaccines, the cost of HPV vaccine is as high as nearly US$ 200. The benefits of HPV vaccines can only be observed in the future, while immediate benefits are seen for many other vaccines. The budget impact for HPV vaccine is relatively large. While most of the other vaccine preventable diseases do not have cost-effective alternative interventions, for HPV infection, there are other cost-effective interventions.

In late 2007, HITAP-IHPP conducted Health Technology Assessments (HTA) using mainly local data to provide evidence to policy makers and other stakeholders. The study funded by the World Bank indicated that the vaccine was cost-ineffective and resulted in vaccine price reduction six months later. These results were used to encourage the improvement of the screening programme for detecting cervical cancers. It was pointed out that market approval of a vaccine is done by the Thai Food and Drugs Authority. The National Vaccine Committee, Thailand, an autonomous institute currently makes recommendation for EPI. The vaccine is purchased by the NHSO. The reality for introducing new vaccines is challenged by the fact that Thai households are willing to pay only 50 000 Baht/QALY for prevention against their willingness to pay 100 000 Baht/QALY for treatment. The current budget for EPI in Thailand is around ~600 million baht. Against this background, the Ministry of Public Health was interested in knowing whether and at which price the vaccine could be cost-saving. Cost-effectiveness league tables of selected interventions used in Thailand and examples of using HTA to inform decisions of the NLEM were also shared.

The HPV vaccine price per dose changed in the market in Thailand from 2006 to 2012. The HITAP's HTA report launched in 2007 has determined the benchmark threshold price at 1 per capita GDP/QALY as 2500 baht per dose. The analysis conducted for the Ministry of Public Health in 2011 determined 190 Baht as the threshold price at which HPV vaccine was cost-saving. The status of cervical screening, the other alternative for HPV vaccine noting that both the annual and cumulative enrolment during 2005–2009 was inadequate was displayed. The presentation concluded with lessons learnt.

Vaccine introduction in Thailand is no longer done by a single health authority, but by the involvement of multiple stakeholders. Given the

limited budget, high-cost of new vaccines, and politics surrounding the introduction of new vaccines, generating economic information has been increasingly important. Therefore, there is a need to have a clear mechanism to facilitate new vaccine introduction and use. Equally important is the need for improving attitudes towards understanding prevention and health promotion among stakeholders in Thailand.

2.9 Global immunization financing: issues and challenges for NUVI

Globally, immunization is considered as a public health priority and key to achieve MDG4; it is a public good and generates positive externalities and collective benefits. Considering it as the most cost-effective health intervention, immunization financing is the responsibility of governments and partners. The following are the key financing issues:

- identifying current cost of national immunization programmes (NIP) and methods of financing;
- estimating :
  - future programme and NVI cost
  - likely availability of resources in the future
  - gap between cost and funding available
  - ways and means of reducing the gap and reaching financial sustainability

Planning, monitoring and reporting tools that include financing information are: comprehensive Multi-Year Plan (cMYP); Joint Reporting Form (JRF); and Annual Progress Report for GAVI.

To achieve financial sustainability, countries need the following:

- efficient use of existing resources;
- mobilize more resources over time;
- increase share of domestic and public resources;
- indicate clearly the resource requirements in annual plans;

- allocate sufficient resources to national budget line for vaccines/ operational cost;
- monitor and evaluate periodically the implementation of annual plans.

To generate and sustain budgetary resources for immunization, it would be necessary to increase health resources from other sectors, efficiency; expenditure from debt reduction; mobilization from domestic revenue; borrowing and aid.

A recent financial analysis in nine Latin American countries has shown that wage cost makes up a large share of the budget of ministries of health and it is controlled by the ministries of finance. The national budget mainly finances delivery costs. The highest share of government expenditure on vaccine was 1.8%, while the lowest was 0.7%. The overall objective of GAVI's co-financing mechanism was to ensure countries putting on a trajectory towards financial sustainability for immunization and enhance the country ownership.

In providing financial assistance for 2012, GAVI has divided the eligible countries into three categories based on the GNI per capita. The level of co-financing varies with these groupings:

- low-income countries: US$ 1005 GNI p.c. (WB low-income country definition);*
- intermediate: US$ 1005 to US$ 1519 GNI p.c.;*
- graduating: US$ 1520 (eligibility threshold) GNI p.c. and above.*

*Revised annually based on World Bank data published in July each year

These country groupings have different policy implications for different categories of countries.

GAVI is supporting low-income countries while ensuring that country ownership and amount per dose will be US$ 0.20. The intermediate group will be supported to move towards financial sustainability starting with US$ 0.20 and then increasing steadily by 15% per year. The graduating countries will be supported for establishing the financial sustainability plans

and help to gradually ramp up over five years (1+4) to reach the projected price after GAVI support ends and will not be eligible for new GAVI support.

Discussion points

- There should be studies to show investments in immunization leading to economic gains by improving productivity.
- Countries of the SEA Region should target for increasing fiscal space for health and immunization.
- Increasing absorption capacity of the immunization programmes should be given high priority to increase HR capacity.

2.10 Vaccine supply update

UNICEF annually procures vaccines and other immunization supplies for more than 100 countries in the world. Vaccine procurement has increased significantly since 2000, and the value of vaccine procured in 2011 exceeded US$ 1.2 billion.

The supply and demand of pentavalent capacity has ramped up since 2001. The pricing trend is declining for both GAVI and non-GAVI countries, but supply market is fragile due to suspensions and de-listing from pre-qualification. This has led to changes in vaccines, shipment plans, and depleting country stocks, but on the other hand, voluntary suspensions of shipments are evidence of functioning Quality Assurance Centre and action by manufacturers themselves.

Sixteen countries have introduced pneumococcal vaccine between December 2010 and December 2011. Out of the 12 countries approved for support by GAVI in 2012, eight countries introduced it by end-2012. Based on the current supply and readiness it is anticipated that 11 additional countries will introduce it in 2013. From the experience of introducing countries pneumococcal vaccine in 2011, it can be concluded that on average 7–8 months are required from supply availability to introduction. UNICEF is currently in the final stages of a tender aiming to secure additional supply capacity, in particular for the short term, to

support 11 more countries approved by GAVI, but awaiting supply before their introduction.

Eight countries introduced rotavirus vaccine during 2011-2012 and all 14 countries currently approved by GAVI for funding support are expected to introduce it in 2013 and 2014, as supplies become available for these countries at the latest during the fourth quarter of 2013. Countries seem to prefer to introduce two-dose vaccines in comparison to three-dose vaccines.

There will be two opportunities for GAVI support for human papillomavirus (HPV) vaccine introduction as national introduction and demonstration projects. A successful demonstration project will be a prerequisite for support to national introduction. The UNICEF tender includes forecasts for graduating countries (current and future).

Current forecasts for measles and rubella vaccines reflect the switch from monovalent measles to measles and rubella (MR) vaccine. Nepal had a catch-up campaign of MR vaccine in 2012 and Bangladesh has planned a MR catch-up campaign in 3rd quarter 2013 pending GAVI final approval, while additional countries of the Region have been projected for introduction for 2014–2016. Supply of measles-containing vaccines generally meets the demand; however, planning in advance and accurate forecasting is important to ensure timely availability of vaccine. As MR continues to be supplied by a single supplier with prequalified product, and as the same manufacturer is at the same time the largest measles vaccine supplier, any changes in demand between measles and MR in particular could require a minimum of lead time of 3–4 months, depending on the requirements, and also country flexibility for registration/licensing. Regarding delivery of injection devices for countries requiring bundled vaccines, especially for campaigns, there is a minimum 3–4 month lead time from the time of order placement to delivery.

Adult diphtheria vaccine and tetanus vaccine (Td/TT) switch will require careful planning and forecasting by countries to avoid a situation like DTP that had shortages. The present supply is sufficient, but adequate availability of either vaccine when needed is dependent on long-term planning for the switch and accurate forecasting by countries. By 2016, all SEA Region countries procuring through UNICEF are projected to have

switched to Td. However, the availability of TT UNIJECT will depend on the existing demand. A lead time of minimum 7–9 months will be required for production and shipment after the receipt of funds.

The switch to bivalent oral polio vaccine (bOPV) from trivalent oral polio vaccine (tOPV) for both SIA and routine settings will be expected to begin in 2015 and fully implemented by 2016, with IPV introduction beginning prior to the switch. For the switch to take place, sufficient licensed bOPV product, as well as low-cost IPV options and supply must be available. This will require very close coordination and planning with the Supply Division, countries and polio programme partners to balance reduction in tOPV production to avoid excess or a shortage of tOPV.

The two WHO pre-qualified products of inactivated oral cholera vaccines (OCV), Dukoral (monovalent OCV in 3ml single dose vial presentation) and Shanchol (bivalent OCV, in 1.5ml single dose vial presentation) have a very limited procurement to date through UNICEF, except for 2012 when 200 000 doses were supplied to Haiti as part of its cholera response plan.

Typhoid vaccine has only one pre-qualified product for polysaccharide vaccine, and so far UNICEF has only procured limited quantities. GAVI has opened a window for typhoid support through the caccine investment strategy (VIS) and is waiting for conjugate vaccine to be pre-qualified before launching this support.

UNICEF Supply Division has recently launched a tender to support middle income countries, which often have difficulties accessing newly developed vaccines at affordable prices, yet whose populations remain highly vulnerable to common vaccine-preventable diseases. The tender, which prioritizes procurement of PCV, rotavirus, and HPV vaccines, aims at establishing more efficient means of MIC access to sustainable supply of new vaccines and at identifying affordable prices to support transparency in the market. Furthermore, it looks at providing an accessible and sustainable mechanism to ensure that, as GAVI-supported MICs graduate from eligibility (e.g. Bhutan), introduction and coverage of PCV, rotavirus, and HPV vaccines can be sustained. This is particularly important for smaller MICs that will not have access to GAVI-pricing beyond 2016 (except through AMC grandfathering) and do not have the same levers as larger

countries, when directly negotiating with manufacturers. There will be two mechanisms for countries to opt into: (1) pooled procurement, where MIC demand is consolidated and procured through UNICEF to achieve better planning and visibility for suppliers (and in return, lower prices for MICs); and (2) reference prices for countries choosing to self-procure to have access to transparent price levels, upon which they may base future negotiations with suppliers. UNICEF's launching of this tender complements the work already done on behalf of MICs in routine and traditional vaccine purchasing. Other vaccines (e.g., polio, pentavalent, measles-containing, and routine EPI vaccines and products) are already procured through existing pooled procurement mechanisms, which most MICs can easily access through UNICEF's Procurement Services.

This engagement in MIC new vaccine procurement is complementing initiatives of other global and regional immunization partners and will be on a time-bound basis, until a healthy market for vaccine procurement develops in the MIC geographies. Participation in the UNICEF pooled procurement system through the MIC tender does not therefore preclude countries from moving to a regional mechanism, if it is established at a later stage.

MICs that have not yet expressed interest but are interested in benefiting from either of the above mechanisms are encouraged to visit the dedicated section on UNICEF's website to obtain further information (http://www.unicef.org/supply/index_67101.html) and communicate their requirements to UNICEF SD as soon as possible, so that they can still be included in the current tender.

2.11 Polio, measles, japanese encephalitis (JE), rotavirus and invasive bacterial diseases (IBD) Laboratory Network

The South-East Asia Region has laboratory networks for polio, measles and rubella, JE, rotavirus and IBD. The networks include a reference laboratory for each disease and national laboratories. India and Indonesia have several numbers of national laboratories due to the large geographical extent that needs to be covered. For polio, the Regional office receives case-based surveillance data of acute flaccid paralysis every week and for measles/rubella, JE (monthly), rotavirus and IBD (quarterly) aggregated data. The polio laboratory network was started in 1993 with three laboratories

and now has expanded to 16, accounts for 60% of the global workload. Indian laboratories process over 90% of the regional workload.

2.12 New and underutilized vaccines (NUV) regulatory challenges and vaccine safety monitoring

The demand for vaccines has increased due to new initiatives and the global coalition efforts and public awareness on vaccine safety, quality and efficacy also has increased through media, internet and other social networks. As a result the implementation of international/WHO regulatory standards also has become highly sophisticated to cater to the demand.

The South-East Asia Region has five countries that are procuring EPI vaccines only through UNICEF (National Regulatory Authority [NRA] with two functions: licensing and AEFI monitoring), two countries that are self-procuring (NRA with two additional functions: lot release and laboratory access) and four countries (NRA with all six functions that include regulatory inspections and clinical trial evaluations). While most of the NRAs vaccine producing countries in the South-East Asia Region do not have optimal capacity, their vaccine pharmacovigilance capacity also needs strengthening.

WHO has developed several tools for strengthening NRA capacity and vaccine pharmacovigilance capacity including surveillance guidelines; vaccine reaction rates information sheets, aid memos and position papers.

Tools and processes available:

(1) translations of standardized case definitions;

(2) simple, easily adaptable AEFI reporting and investigation forms;

(3) a standard set of core variables to be incorporated into AEFI surveillance and investigation;

(4) reporting tools;

(5) e-learning basic and advanced courses (www.vaccine-safety-training.org);

(6) vaccine pharmacovigilance toolkit;

(7) resource materials at Programme for International Drug Monitoring.

Priorities set for end 2013

(1) Intensifying NRA capacity building activities in priority countries with no PQ vaccine production i.e.: Bangladesh, Myanmar, Nepal; team up with small size country i.e.: Bhutan, Maldives - two phases process; 1) self-assessment followed six months to one year later with two - formal assessment with external consultants;

(2) Institutionalizing production of regional working reference standards for the testing of vaccines (India, Indonesia, Thailand extended to China and Viet Nam);

(3) Conducting NRA assessment and preparation of institutional development plan for post-marketing surveillance (PMS) as part of the overall NRA capacity building;

(4) Pilot project in Indonesia and India to address under-reporting of AEFI in a systematic way;

(5) Support to countries to update national guidelines and to facilitate AEFI training workshops at subnational levels;

(6) Regional consultation on AEFI causality assessment.

Discussion points

- There should be a mechanism to share AEFI information and experience in managing events among countries of the Region.
- The South-East Asia Region should develop a road map for implementing "pool procuring of vaccines": national programme managers should start discussing the need and feasibility with in-country authorities.
- The process of pool procurement requires harmonization of multiple good manufacturing processes before moving to group/pool procurement.

2.13 NITAG (NCIP) and EPI Team's role in decision-making in immunization

The Global, Regional and National Immunization Policy Advisory Framework includes functions of the Strategic Advisory Group of Experts (SAGE), other WHO Technical Advisory Committees at the global level, Regional Technical Advisory Group and National Immunization Technical Advisory Group (NITAG).

The guiding principles of the Global Immunization Vision and Strategy (GIVS) were highlighted with emphasis on ownership, partnership, responsibility and policies and strategies based on evidence and best practices.

In relation to the Decade of Vaccines and the Global Vaccine Action Plan ratified at the Sixty-fifth World Health Assembly in May 2012, it was reminded its first strategic objective that all countries should commit to immunization as a priority. It was quoted that national legislation, policies and resource allocation decisions should be informed by credible and current evidence regarding the direct and indirect impact of immunization. Attention was drawn to the point indicated under the first objective that independent bodies such as regional or national immunization technical advisory groups (NITAGs) to guide country policies and strategies should be established or strengthened.

NITAG has a technical advisory role for all vaccine-preventable diseases and should not serve as an implementing, coordinating or regulatory body. Interagency Coordinating Committees (ICCs) were not equivalent to NITAGs.

NITAG's role in strengthening EPI programmes included independent technical input with broad expertise, allowing for an evidence-based review and decision for an increasingly complex area, allowing more comprehensive and cohesive country immunization programme perspectives, adaptation of global policy recommendations with consideration of local epidemiology and social contexts, ensuring credibility and organizations' buy-in and acceptance of the programme, demonstrating country ownership and important elements of other DoV-GVAP guiding principles such as sustainability, shared responsibility, partnership, equity,

integration, sustainability and even innovation and monitoring the GVAP implementation.

The six basic process indicators included in the UNICEF/WHO Joint Reporting Form are used as part of the GVAP monitoring and evaluation framework to review the existence of a functional NITAG, and additional process, output and outcome indicators are available for use by regions and countries. Based on the six basic process indicators, the performance of NITAG in the Region was reviewed. Next, the 10 process indicators determining the functionality of a NITAG, based on global recommendations and best practices were introduced to participants.

Guidance and resource documents, exchange of experience, technical support and Supporting Independent Immunization and Vaccine Advisory Committees (SIVAC) resource centre were highlighted as ways of WHO and partners support for strengthening NITAGs.

An update on the situation in the South-East Asia Region was provided. A series of consultative workshops were conducted by WHO for the members of the NCIPs (Nepal in 2009, Indonesia in 2010, Bhutan in 2011 and Myanmar in 2012) with the support of SIVAC (through IVI) and CDC Atlanta. Nepal and Bhutan had developed NCIP charters. The role Nepal NCIP played, was explained including their organizing a series of consultations for deciding strategies for expanding JEV, introducing rubella, discussing the feasibility of introduction of Rota and pneumococcal vaccines and the planned HPV vaccine workshop in early 2013. Bhutan conducts regular quarterly meetings to discuss different issues.

Highlighted issues and challenges were the independency of advisory bodies, lack of expertise in smaller countries, majority members being government employees, lack of state or regional representation in large countries, some partner-driven EPI activities, limited capacity and lack of funds. In conclusion, extracts from the NCIP, Nepal containing the terms of reference of the committee, preparation of agenda and background materials, procedures related to preparing and sharing minutes, declaring conflicts of interests, acting of a member in a discussion involving conflicts of interests and ensuring confidentiality of matters dealt with were shared.

3. Group discussions

The participants were divided into three groups. Group I comprised participants from Bangladesh, India and Nepal while Group II comprised those from Maldives, Sri Lanka and Thailand. Group III consisted of Bhutan, Indonesia, Myanmar and Timor-Leste participants. The groups identified disease burden, efficacy and safety of the vaccine, affordability, sustainability, programme capacity, equity and availability of domestic or regional vaccine production capacity, as important criteria for consideration for prioritizing new and underutilized vaccines and deliberated further in identifying the important barriers in using each criteria and proposed the means to overcome the barriers.

3.1 Summary of group discussions

Criterion	Barrier	Means to Overcome
Disease burden	➢ inadequate – quantitative/qualitative data – systems to collect information and validate data ➢ ill-defined threshold limits ➢ irrelevant global/ regional estimates of data	➢ establish/strengthening sensitive public health surveillance ➢ strengthen laboratory support system ➢ maximize use of available information including evidence based findings ➢ capacity development ➢ Establish local expert groups ➢ local research
Efficacy of the vaccine	➢ inadequate – country context evidence/data – capacity to conduct clinical trial	➢ expert group for assessing available efficacy and safety of available data/evidence ➢ development of sites and capacity for clinical trials
Safety of the vaccine	➢ inadequate post marketing surveillance (PMS) data	➢ strengthen the AEFI surveillance ➢ improve NRA capacity ➢ networking among countries ➢ pilot introductions to learn more

Criterion	Barrier	Means to Overcome
Affordability	➢ high cost of vaccine in comparison to per capita income	➢ mobilize external funding for initial period ➢ negotiate with the manufacturer for price reduction ➢ explore new sources of income for financing immunization ➢ make available adequate information on feasibility, effectiveness and coverage ➢ implement standardized methods of cost effectiveness and cost-saving studies
Sustainability	➢ inadequate resources ➢ lack of political commitment and policy analysis	➢ funding for immunization (vaccines) as a line item in the national budget ➢ policy dialogue and evidence-based findings dissemination among the policy-makers
Programme capacity	➢ inadequate – human resources: strength & capacity – cold chain capacity – planning and forecasting – supply chain management ➢ ineffective communication ➢ lack of an accountability framework	➢ human resource development and deployment with managerial capacity ➢ communication and social mobilization ability ➢ an accountability mechanism ➢ inventory management ➢ include private sector in delivering appropriate vaccines
Equity	➢ lack of focus to highlight equity in vaccine access and delivery	➢ raise the issue at all levels of discussions

4. Polio endgame strategy

Subsequent to the consultation on new and underutilized vaccine introduction, a discussion on inactivated polio vaccine (IPV) and a consultation on the polio endgame strategy in the South-East Asia Region (SEAR) were held. The general objective of the consultation was to review

and discuss proposed strategies for maintaining the polio-free status in the Region following global polio-free certification. The specific objectives focused on (1) reviewing the current status and progress of polio eradication and certification in the Region; (2) reviewing the global polio endgame strategy; and (3) developing a road map for the regional polio endgame strategy.

The participants were briefed on the polio endgame strategy which entailed differential risk management, strategies for post-OPV surveillance, choice of the vaccine, vaccine supply and management, financial support and sustainability. In relation to the choice of vaccine, it was highlighted that the continued use of oral polio vaccine (OPV) after interruption of wild poliovirus transmission is inconsistent with the idea of polio eradication as OPV may cause, in rare instances, vaccine-associated paralytic polio (VAPP) and potentially lead to outbreaks of circulating vaccine-derived poliovirus (cVDPV).

The discussion on Polio Endgame Strategy and switch from tOPV to bOPV (type 1 & 2) plus IPV focused on issues related to IPV and reviewed its role as a tool for polio eradication and specifically, the polio endgame strategy. The Polio Endgame Strategy referred to the risk mitigation activities related to the withdrawal of the oral polio vaccines. The current strategy involves a global switch from tOPV to bOPV with at least a single dose of IPV. In this context, the consultation deliberated on (1) how the Polio Endgame Strategy for the South-East Asia Region could be operationalized, and (2) how each country should approach the polio endgame to include vaccine options for the switch.

For more details of the polio end game strategy and switch from tOPV to bOPV plus IPV, please refer to the report of the South-East Asia Regional Consultation on the Polio Endgame Strategy.

5. Conclusions

(1) In light of the WHA 65.18, the Global "Immunization Week" planned in April could be used as one of the strategies for further intensifying routine immunization beyond 2012.

(2) Member States of the SEA Region have more than 10 years of experience of introduction of new and underutilized vaccines. There continues to be substantial technical and financial support available to Member States (WHO, UNICEF, GAVI, BMGF and CDC).

(3) The environment for NUVI is complex. Member States should not wait to build the capacity of the national EPI programme before introducing new and underutilized vaccines, but should instead use NUVI as an opportunity to strengthen their systems. While doing so, the overall health system gaps should be assessed and taken into account.

(4) Small countries find it difficult to generate their own disease burden data.

(5) Experience in other regions has shown that herd immunity is an important issue to be considered in the decision-making process for introducing new vaccines (e.g., PCV and rotavirus vaccines).

(6) Priority vaccine for introduction during the next 3–5 years should be HPV, rotavirus, PCV, typhoid, cholera, and IPV. However, at the country level, it should be subjected to the application of the final decision-making algorithm, (Annex 4).

(7) While there is a need to increase fiscal space for health and immunization, the case can be made for an investment in health. However, all countries that receive financial support struggle with lack of human resource and poor utilization capacity.

(8) The actual drive for bringing down vaccine costs is not increased demand, but competitive market forces.

(9) Post-marketing surveillance data and other relevant information is important and should be available for NRAs that want to license vaccines.

(10) NRA practices should be harmonized to allow standardized vaccine licensing mechanisms to be developed in the Region.

6. Recommendations

For WHO

Assistance should be provided to Member countries to:

(1) develop a tool to closely monitor the implementation of IRI including NUVI activities at all level of immunization services and finalize the decision-making algorithm for NUVI;

(2) document their experience with the introduction and impact of Japanese encephalitis and hepatitis B vaccines;

(3) develop a road map for implementing pool procurement mechanisms for vaccines, particularly for the small and self-procuring countries (e.g., reliable access due to small volume, and issues related to licensing by the NRA); noting the pool procurement model for middle income countries implemented by UNICEF, which could be of interest;

(4) document the economic and productivity gained through high coverage immunization programmes;

(5) develop mechanisms for sharing AEFI information and experiences, as well as a package of strategies to communicate with the public about vaccine safety (pro-vaccine lobbying);

(6) continue AEFI causality assessment capacity building and develop regional expertise.

For Member Countries

Attention should be paid to the following:

(1) ensuring political commitment and quantifying human resource, financial needs, communication, cold chain and logistic requirements;

(2) aligning and integrating the strengthening of routine immunization and NUVI with the eradication and elimination goals as well as with other communicable and noncommunicable disease programmes;

(3) improving post-marketing vaccine surveillance, particularly in detecting, managing, investigating and reporting of AEFI cases.

(4) Countries not having the capacity to generate their own disease burden data should use data from neighbouring countries or regional data to facilitate their decision-making process.

Annex 1

Opening remarks
Dr Samlee Plianbangchang,
Regional Director, WHO South-East Asia

Distinguished participants, ladies and gentlemen,

I warmly welcome you all to the Regional Consultation on Introduction of New and underutilized Vaccines. I thank you very much for your time.

Worldwide, it was estimated in 2011 that 6.9 million children died before their fifth birthday. This was compared to around 12 million in 1990. Child mortality rates have fallen in all regions of the world during the last two decades, and are down by at least 50%. The decreasing rate of under-five mortality during the period from 1990 to 2000 was 1.8%, and it was 3.2% between 2000 and 2011.

Most children die from preventable causes. The gains in child survival, although significant, are still insufficient to achieve the MDG4 of reducing the global under-five mortality rate by two thirds between 1990 and 2015. Globally, the leading causes of death among under-five children are pneumonia, diarrhoea, birth complications, including pre-term, and malaria.

Launched in 1974, the Expanded Programme of Immunization (EPI) was first designed to deliver immunization services against diphtheria, tetanus, pertussis, poliomyelitis, measles, and tuberculosis (BCG).

Together, these vaccines have prevented close to 2.5 million deaths every year. Now, with the addition of hemophilus influenza, pneumoceocal, and rotavirus, it is estimated that immunization may directly contribute to about 25% reduction in childhood mortality.

In the WHO South-East Asia Region (SEAR), significant progress has been made in protecting children against vaccine-preventable diseases. Still, some 10 million children do not receive DPT3 vaccination during the first year of life.

Therefore, the Sixty-fourth Session of WHO Regional Committee for SEA adopted a resolution declaring 2012 as "the Year of Intensification of Routine Immunization in the Region". The resolution was based on the recommendation of the High-Level Ministerial Meeting held in August 2011. I am pleased to note from the report of the recently held Regional Review Meeting of EPI Programme Managers that country plans have been developed to intensify routine immunization, as per the Regional Committee resolution, and that their implementation is under way.

Furthermore, the recent years have seen a dramatic increase in the introduction of new and under-utilized vaccines. These vaccines include hepatitis B, hemophilus influenza, type B (Hib), streptococcus pneumonia, rotavirus, and rubella.

Vaccines against a number of important public health diseases have also been developed or improved. Proper use of vaccines, such as those against Japanese encephalitis, meningococcal meningitis and typhoid can further decrease the disease burden in poor countries. Besides, vaccines against TB, malaria, and dengue are at various stages of development.

Building on the success of national immunization prgoramme (EPI) the wide use of new and under-utilized vaccines has the potential to significantly contribute to the achievement of MDG4. However, adding new vaccines to the routine immunization (RI) schedules requires careful considerations. Several critical issues must be thoroughly scrutinized, including the ability of governments to afford vaccines in the long term. The other considerations fall in areas such as decision on priority vaccines, capacity of the immunization system to absorb additional vaccines, equitable distribution of new vaccines, plan to ensure long-term availability of vaccines, and integrating the use of vaccines into the broad context of national disease prevention and control strategies.

Most SEAR countries do not have the means to access and evaluate the newly developed vaccines. In view of the remarkable differences among countries in their resource capacities, and ability to prioritize vaccines for maximum cost-benefits, WHO held a workshop on Vaccine Prioritization in 2009 at which a priority list of vaccines was developed. The list also includes a clearly defined set of criteria that countries should use in their considerations prior to making a decision on the choice of new vaccines. Whatever the situation, Member States are still facing difficulties in making such a decision primarily because of lack of adequate

evidence on disease burden, inability to expand and maintain the cold chain capacity, and limitation of resources, including human resources.

Knowing that the introduction of new vaccines presents numerous issues for a national immunization programme especially in prioritizing investments in the light of limited national resources, it is a challenge to tackle such issues in a systematic manner to ensure availability of the most cost-effective immunization services.

Ladies and gentlemen, while accepting that vaccination is the best intervention to reduce or eliminate childhood diseases, and also that it is beyond the ability of governments to afford vaccination, especially in the long term, we should resort to other public health interventions to protect the health of children. Such interventions could be food and nutrition, water supply and hygiene and sanitation, as well as other aspects of environmental health.

With these words, ladies and gentlemen, I wish you all a productive consultation and a pleasant stay in Bangkok. Thank you

Annex 2

Agenda

(1) 2012 the Year of Intensification of Routine Immunization in the South-East Asia Region

(2) Framework for new and underutilized vaccine introduction (NUVI) in South-East Asia Region

(3) Global scenario of under-five mortality: Potential contribution of vaccines including NUV for achieving MDG 4

(4) 12-year regional experience of NUVI- lessons learnt and issues

(5) NUV I – Global implementation status and issues with focus on pneumococcus, rotavirus, HPV, cholera and typhoid vaccines

(6) AES/AMES surveillance in SEAR, with focus on JE

(7) Multi-country JE vaccine adoption project

(8) Forecasting availability and pricing trends of NUV – HPV, pneumococcus, rotavirus, typhoid, cholera, IPV, tOPV, mOPV and bOPV

(9) Global immunization financing : Issues and challenges for NUVI

(10) Health systems strengthening: issues and challenges for NUVI in the South-East Asia Region

(11) NUV regulatory challenges and vaccine safety monitoring

(12) Future GAVI perspectives for policy and implementation of NUVI

(13) Strengthening laboratory network and expansion of polio measles JE rotavirus & IBD surveillance to other diseases covered by priority NUV

(14) Role of NCIP (NITAG) and EPI teams in decision making for NUVI post-polio eradication and polio vaccines

(15) Polio Endgame Strategy

Annex 3

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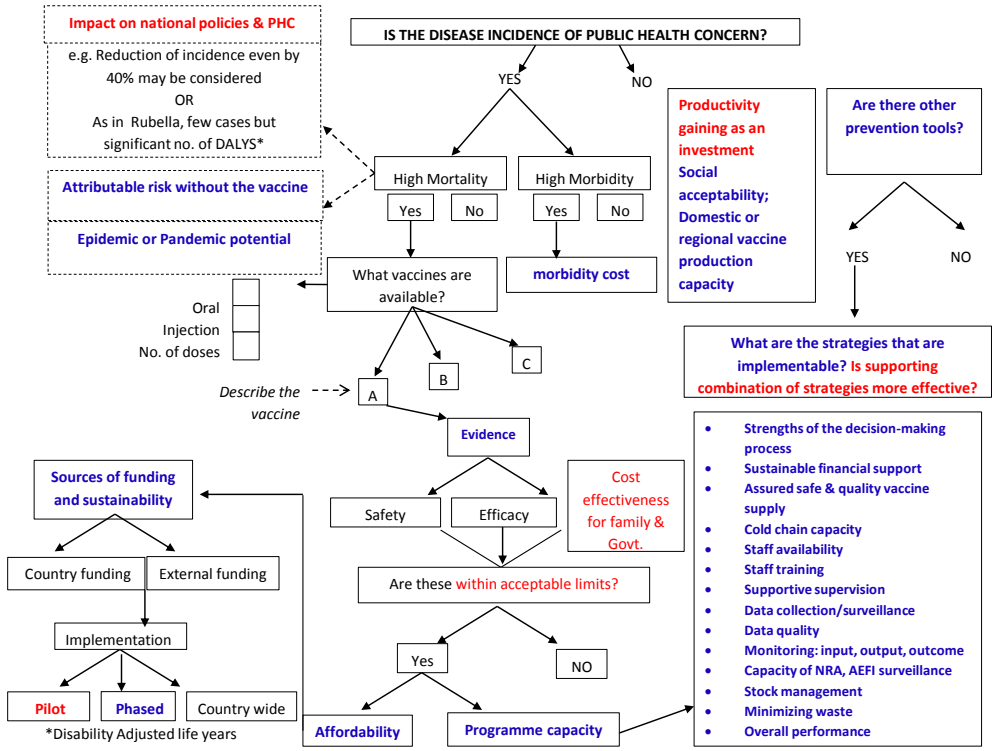
Annex 4

Draft algorithm for decision–making for introduction of new vaccines



The Regional Consultation on Introduction of New Vaccines in the South-East Asia Region was held on 11–13 December 2012 in Bangkok, Thailand. The primary objective of the Consultation was to agree on a regional framework in the South-East Asia Region that will enable Member countries to make rational decisions on new vaccine introduction.

The consultation brought together the key technical experts and EPI managers from Member States of the WHO South-East Asia Region for this purpose and reviewed the existing criteria and agreed for a draft decision-making algorithm for countries to use at the national level in introducing new and underutilized vaccines in the future.

This publication contains the report of the above consultation. The report includes a review on the progress of the implementation of "2012-Year of Intensification of Routine Immunization", regional decision-making framework for new and under-utilized vaccines (NUVI), potential contribution from NUVI in achieving millennium development goals (MDGs), the global and regional new vaccine introduction experience, Japanese encephalitis and acute encephalitic syndrome surveillance, issues and challenges of health system strengthening for NUVI, public health benefits of NUVI in Thailand, issues and challenges of sustaining immunization financing, an update on vaccine supply, polio, measles, Japanese encephalitis, rotavirus and invasive bacterial disease surveillance, regulatory challenges for NUVI and roles of national committees of immunization practices and national expanded programme on immunization in decision- making for NUVI.

This report makes recommendations for Member States of the WHO South-East Asia Region on their efforts to achieve the Global Immunization Vision and Strategy (GIVS) goals.

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