Typhoid vaccine use in countries – progress and challenges:

Feedback from the regions and countries on the implementation of SAGE recommendations on typhoid vaccines

Meeting of the Strategic Advisory Group of Experts, SAGE

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World Health Organization
Purpose of this report

In your deliberation on typhoid vaccines in November 2007, several important recommendations were made. And one of the key follow up action required was

- "SAGE emphasized the need for feedback from WHO’s regional offices and countries to determine how countries could implement SAGE’s recommendations. SAGE anticipates that these responses will be available within 12–18 months." *WER No. 1, Jan 2008, 83, 1–16*

*This report summarizes the feedback from the regions and the countries, and also the current status on the use of typhoid vaccines globally*
Prioritization and engagement with Regions and countries

- Reviewed the currently available data on typhoid disease burden, and information on vaccine use in countries

- Communicated with regional advisers
  - In PAHO, only Cuba has a routine typhoid vaccination programme
  - No country in AFR has expressed interest in typhoid vaccination, largely because the disease burden is unknown
  - Only Pakistan in EMR, and Kyrgyzstan in EUR has shown interest

- Priority focus;
  - SEAR, followed by WPR, and on a limited scale EMR and EUR
## Reporting of typhoid vaccine use in the WHO/UNICEF JRF

<table>
<thead>
<tr>
<th>WHO Region</th>
<th>Country</th>
<th>Target vaccine recipient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa Region</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>Region of the Americas</td>
<td>Argentina, Brazil, Cuba</td>
<td>Army, Special groups 10, 13, 16 years</td>
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<tr>
<td></td>
<td>Argentina</td>
<td>High risk groups</td>
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<tr>
<td></td>
<td>Brazil</td>
<td>Food handlers</td>
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<tr>
<td></td>
<td>Cuba</td>
<td>Food handlers</td>
</tr>
<tr>
<td>Eastern Mediterranean Region</td>
<td>Iraq, Kuwait, Oman, Qatar, Saudi Arabia, United Arab Emirate</td>
<td>High risk groups, Food handlers, Food handlers, Groups not specified, Food handlers</td>
</tr>
<tr>
<td>European Region</td>
<td>Cyprus, Kazakhstan, Slovenia, Uzbekistan</td>
<td>Only if specific indications, High risk groups, Only if specific indications, High risk groups</td>
</tr>
<tr>
<td>Western Pacific Region</td>
<td>Brunei Darussalam, Malaysia, Republic of Korea, Viet Nam</td>
<td>Not specified, Food handlers, High risk groups, Part of the country</td>
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Engagement with the Regions and Countries

- Visits to Regional Offices; two visits to SEA Region

- Country visits
  - Nepal (Feb 2010), India (Feb 2010), Bhutan (June 2010), China, Guangxi (June 2010), Fiji (Aug 2010), Sri Lanka (Oct 2010)
  - For Pakistan and Kyrgyzstan, long discussions through WHO country and Regional Offices

- Typhoid on important global, regional and country meetings
  - Global
    - DEVAC, Malaga (Oct '09), GAVI Partners Forum, Hanoi (Nov '09), GVRF, Mali, (Nov '09), GIM, Geneva (Feb '10), NUVI Meeting, Montreux, (Jun '10)
  - Regional
    - SEA ITAG (Jul '08), SEAR EPI PM meeting, (Aug '08), Bangkok Meeting (IVI), (Mar '09), SEAR EPI PM & Pandemic Focal Points Meeting (Sep '09), SEA EPI PM meeting (Jul '10)
  - At meetings of country Immunization TAGs,
    - Pakistan, India, Bhutan, Nepal
Program strategy

- **Routine EPI schedule and typhoid vaccination**
  - The Delhi state programme of ViPS vaccination shows that typhoid vaccination can also be easily integrated into the current routine EPI programme
  - But typhoid vaccines provide an opportunity to realise GIVS Strategic Area 1, *Protecting more people in a changing world by Expanding vaccination beyond the traditional target group*.

- **School-based strategy**
  - It is an acceptable strategy successfully used in China, planned for Fiji

- **Risk-based strategy**
  - The real issue is defining the risk areas or groups as most countries have either no surveillance or weak surveillance systems in place

- **To assist with decision analysis, an introduction tool for typhoid vaccines is in development**
Outbreak control

- Experience from China on the use of ViPS vaccine to control typhoid outbreak is well documented.
- Pondicherry, India, following the 2004 Tsunami, used ViPS as a preventive vaccination campaign targeting primarily children below 5 years of age. No typhoid cases were reported in Tsunami affected areas.
- Following the Pakistan earthquake in 2005, a pediatric Vi vaccination campaign was undertaken in affected camps with over 50,000 doses administered. No cases were recorded in the camps in question over the following 4-6 months in routine surveillance.
- Cyclone Tomas struck North and North-Eastern part of Fiji in March 2010. By June a mass campaign to reach 70,000 people in typhoid endemic areas with the ViPS vaccine
Vaccines and tools

- Vaccines options-injectable vs. oral
  - If cost is not an issue, some countries are interested in the oral vaccine
  - Limited duration of protection & need for repeat doses present costs and logistics challenges to countries considering these vaccines

- Surveillance
  - All countries have a morbidity/mortality reporting system and most of them include typhoid. However, the terms typhoid and enteric fevers are not well defined in such reports
  - Blood culture facilities are not available in most health facilities, particularly in the periphery of the health infrastructure networks, and simple diagnostic kits are not widely available.
  - There is no example of sentinel surveillance targeting pre-school and school-aged children
S. Typhi vs S. Paratyphi

- Experience from Thailand as well as China show that as S. Typhi incidence declines, there is a concomitant rise in the incidence of S. Paratyphi.
  - Un-masking effect or replacement phenomenon??

- Guilin, China, rising paratyphoid cases- people doubting value of typhoid vaccination, active promotion of typhoid vaccine halted

- In Nepal, the proportion of S. Paratyphi was 32.9% and 62.5% in 2007 and 2008, respectively

- In the absence of a vaccine against S. Paratyphi, many countries are uncertain whether introduction of a vaccine against S. Typhi would have any impact at all on enteric fevers
WHO prequalification of typhoid vaccines

• WHO prequalification of a vaccine is vital if uptake is to be accelerated

• Prequalification process for three typhoid vaccines produced by different manufacturers have been initiated.
  – Two out of three are ViPS
  – The third one is the live oral attenuated Ty21a vaccine.

• Currently the prequalification of one of the polysaccharide based vaccines is expected by October-November 2010.

• The live oral attenuated vaccine is advanced in the process and prequalification may be expected early 2011.

• The third vaccine is still on the initial stages of the process but prequalification may be expected by 3Q 2011
Recent introductions

- **Delhi**
  - Started in 2004, had some start-up problems, but since 2007, running smoothly
  - ViPS used, one dose for 2-5 year old, average about 300,000 children immunized annually
  - ViPS manufactured in India

- **Fiji**
  - Cyclone Tomas in March 2010, sudden rise in typhoid cases seen
  - A campaign in the high risk areas to immunize 70,000 people
  - Plan for routine programme as a school-based strategy,
  - Vaccinating food handlers as well

- **Sri Lanka**
  - Their own production of whole cell killed vaccine stopped around 2003
  - Last year re-started use of ViPS sourced from India with 20,000 for an outbreak
  - For 2010, procured 200,000 doses
  - October visit; suggested to refine the surveillance and focus on "hot spots" in North of the country
Definite plans to introduce

- **Nepal**
  - Typhoid and cholera are well entrenched across Nepal, high on government agenda
  - Intent on addressing it, both together if possible
  - Have a relative good surveillance in place
  - Next meeting planned for 13-14 December to decide on how to go forward
  - Financial Resources is the main issue

- **Bhutan**
  - Regular focal outbreaks in several districts
  - Want to strengthen surveillance in capital city, and
  - Explore possibility of introducing the vaccine in one of the districts where outbreaks are regular; Interested in oral vaccine if affordable
  - Issue of resource

- **Kyrgyzstan**
  - Want to conduct a pilot introduction with oral vaccine
  - Discussion with country office and regional office, but before a country visit to finalise, political turmoil put activities on hold
New Initiatives

- IVI pilot studies in Nepal and Pakistan (VIVA project)

- Multi-Country Typhoid Fever Surveillance Program (TSAP) in sub-Saharan Africa,
  - an initiative by IVI.

- Coalition against Typhoid, (CaT),
  - a consortium led by the Sabin Vaccine Institute

- There will be brief presentations on both later on
Challenges

- **Show me the money**
  - To support countries to strengthen surveillance if the goal of a risk-based strategy is to be implemented successfully
  - To support countries to kick-start vaccination programme
  - To support the cost of vaccines

- The importance of strengthening surveillance for typhoid and the resources needed to do so

- **Diagnostic tool**
  - An affordable, accurate and simple diagnostic tool is essential

- **Better vaccines**
  - Will conjugate vaccines be the answer or
  - Making the current ones affordable

- **Risk-based strategy & the unpredictability of Forecasting**
  - These days a lot of emphasis on forecasting
  - When you don't have data, defining risk area is challenging and that makes forecasting difficult
  - There will always be uncertainty

- **Next stage; Africa**
  - Without resources, not much returns can be expected even if evidence is generated
## Conclusions

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<tr>
<th>Conclusions</th>
<th>Actions</th>
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<td>Despite the lack of global commitment of resources for typhoid, and despite the challenges of currently available vaccines, several countries in the Asia-Pacific Region have taken steps to introduce typhoid vaccines, albeit on limited scales</td>
<td>• Continue to provide technical assistance to these countries to monitor the impact of vaccination</td>
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<td>• There is definite interest in the government of countries endemic for typhoid to explore vaccines as an option to control typhoid, but financial resources is an obstacle</td>
<td>Support establishing typhoid surveillance programmes that can generate credible data and help define better risk areas and risk groups</td>
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<td>• There is definite interest in the government of countries endemic for typhoid to explore vaccines as an option to control typhoid, but financial resources is an obstacle</td>
<td>Explore for global financial commitments to support typhoid programme</td>
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<td>• Lack of a simple, accurate and affordable diagnostic test is a major drawback in defining risk areas and risk groups to target vaccines better</td>
<td>Accelerate communication &amp; advocacy efforts</td>
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<td>• The changing epidemiology of typhoid and paratyphoid presents special challenges for typhoid control in the absence of a vaccine against paratyphoid</td>
<td>• Invest in the development and field testing of alternative diagnostic tests that are accurate, simple and affordable</td>
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<td>• Invest and accelerate the development of not only better typhoid vaccines but also paratyphoid vaccine</td>
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Acknowledgement

- Sabin Vaccine Institute, Ciro de Quadros
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- The EPI Programme Managers in countries
- Members of the Coalition against Typhoid