Proposal for a Workshop

Pre-vaccination screening for the use of dengue vaccines with differential performance dependent on serostatus: rapid diagnostic tests and implementation strategies

Background:

Dengue is a major public health problem with more than 3.6 billion people at risk for dengue virus (DENV) infection and an estimated 390 million infections annually in over 120 tropical and sub-tropical countries. In the absence of truly effective and sustainable vector control measures, a dengue vaccine is urgently needed. The first dengue vaccine was licensed in 2015; the live attenuated recombinant tetravalent vaccine CYD-TDV. However, new evidence highlighted the serostatus-dependent vaccine performance of CYD-TDV; a retrospective analysis of clinical trial data, stratifying participants according to their dengue serostatus before the first vaccine dose, revealed an excess risk of severe dengue in seronegative vaccine recipients, while in seropositive vaccine recipients, the vaccine was efficacious and safe. Whether this serostatus-dependent vaccine performance will also be observed for the second-generation dengue vaccines is currently unknown. However, a differential performance based on baseline serostatus is theoretically possible for all live dengue vaccines.

SAGE provided revised recommendations in April 2018 on how best to use this vaccine in populations at risk:[1] Countries considering the introduction of CYD-TDV should only do so if the minimization of the risk in seronegative individuals can be assured. The pre-vaccination screening is the preferred strategy as with such a strategy predominantly persons with evidence of a past dengue infection would be vaccinated (based on an antibody test, or on a laboratory confirmed dengue infection in the past).

To support a pre-vaccination screening strategy, WHO and many expert panels highlighted the urgent need for rapid diagnostic tests (RDT) to determine serostatus. To date, no RDT has been licensed for the indication of determining dengue serostatus, eg past dengue infection. Pre-vaccination screening strategies will require RDTs that can be done at point of care, provide rapid test results, are sensitive and specific, as well as inexpensive for use in a population wide programme.

[1] http://www.who.int/immunization/sage/previous/en/index.html

In addition to target product profiles for such RDTs, policy-makers need to think through the risk-benefit of diagnostic tests, given that there will always be a certain trade off between sensitivity and specificity. What level of sensitivity and specificity is good enough, which trade-offs are acceptable by communities and governments, how much evidence is needed, and does one need standardized risk classification? Public acceptance of a certain level of specificity will depend on background seroprevalence, co-circulation of other flaviviruses, and the epidemiological situation of dengue in any given country. Optimal age targeting is another aspect that will differ from country to country depending on the peak of hospitalizations seen. Furthermore, both the pre-vaccination screening require careful planning around communication, implementation strategies, acceptability to stakeholders and communities, and cost-effectiveness studies.

Objectives of the meeting:

(1) Assess rapid diagnostic tests (RDT) for screening for past dengue infection

- Discuss the target product profile for RDTs to support a pre-vaccination screening strategy
- Present a landscape analysis on RDT characteristics, and their sensitivity and specificity in different flavivirus endemic settings
- Elaborate on population level benefit versus individual risk
- Address policy-makers` perceptions and views on risk-benefit assessment of an RDT as a pre-vaccination screening tool under different scenarios (high versus low seroprevalence)

(2) Discuss implementation strategies for pre-vaccination screening programmes for dengue vaccines

- Discuss practical issues for programmatic roll-out
- Address the optimal age for vaccine introduction
- Discuss communication strategies with regards to vaccine confidence, both for policy makers, the medical community and the lay public
- Elaborate on school based campaigns versus other facility-based programmes

Target audience:

NITAG experts, EPI managers, policy-makers with experience in vaccine introduction, front-line academic and public health scientists with expertise in vaccine introduction and mass vaccination, industry, diagnostics manufacturers, leaders of laboratory networks, regulatory authorities; WHO; CDC.

Venue: Les Pensieres Center for Global Health, Annecy, France

Dates: 14-16 January 2019

Scientific Committee:

Duane Gubler, Annelies Wilder-Smith, May Chu, In Kyu Yoon, Cassandra Kelly-Ciro, Anna Durbin

Meeting Report: Isabel Delrieu (in charge)

Scientific publication in a peer-reviewed journal: Annelies Wilder-Smith (in charge)

Programme:

	Day 1 – Opening	
14:00-14:10	Welcome	Fondation Merieux Chair : Duane Gubler
14:10-14:30	CYD-TDV dengue vaccine : Long-term safety data stratified by serostatus	Peter Smith, UK
14:30-14:40	Rationale for pre-vaccination screening strategy for dengue vaccine: WHO recommendations	Annelies Wilder-Smith, CH
14:50-15:00	**Discussion**	
15:00-15:20	Dengue vaccine introduction in the Philippines : lessons learned	Maria Wilda Silva, Philippines
15:20-15:30	**Discussion**	
15:30-16:00	BREAK	
16:00-16:20	HPV introduction in Brazilian schools: lessons learned for dengue vaccine introduction	Ana Sartori, Brazil
16:20-17:10	Communicating risk while building confidence in dengue vaccines the context of a pre-vaccination screening strategy	Heidi Larson, UK
17:10-17:30	**Discussion**	
17:30-18:30	BREAK	
18:30	**Key Note Lecture**	
18:30-19:10	**Population benefit versus individual risk of vaccines**	David Curry, US
19:10-19:30	**Discussion**	
19:30	Dinner	

	Day 2	
	POC RDTs and their implementation : TPP	**Chairs : In-Kyu Yoon and May Chu**
8:30-8:50	2018 WHO meeting on flavivirus diagnostics advancement: a summary report of key recommendations	May Chu, US
8:50-9:10	Systematic Review on available RDT for diagnosing dengue serostatus	Robert Luo, US
9:10-10:30	Available RDT landscape analysis : Manufacturers`panel (Chembio, SD Biosensor, Blusense) **Panel discussion**	Diagnostic manufacturers
10:30-11:00	BREAK	
11:00-11:30	Sanofi Pasteur`s validation efforts for different RDTs against existing panels	Sanofi Pasteur, France
11:30-11:45	Discussion	
11:45-12:30	**Discussion**: Target Product Profiles for RDTs for dengue serostatus	Robert Luo, US
12:30-14:00	LUNCH	
		Chairs: Peter Smith and Duane Gubler
14:00-14:25	Modelling different sensitivity/specificity scenarios in different seroprevalence settings : impact on cost and effectiveness of dengue vaccines	Stefan Flasche, UK LSHTM
14:25-14:55	Model-based assessment of public health impact and cost-effectiveness of routine pre-vaccination screening strategy with Dengvaxia®	Guido Camargo España US
14:55-15:15	Ethical deliberations on imperfect RDTs that could lead to inadvertently vaccinating seronegative persons	David Curry, US
15:15-15:30	**Discussion**	
15:30-16:00	BREAK	
16:00-16:45	Break-out session: Which thresholds for test sensitivity and specificity are acceptable by policy-makers and communities?	**Chairs: Sabine Dittrich and Stefan Flasche**
16:45-17:30	**Feedback from Working Groups**	Working group: Asia Working group: Latin America
17:30	DAY 2 – Close	

	DAY 3	
08:30-9:00	Bringing RDTs for dengue serostatus into the market	Sabine Dittrich, FIND Switzerland
9:00-10:30	Programmatic strategies for a CYD-TDV test & vaccinate program : school programmes versus other settings · PAHO Break out o Brazil, Colombia, Peru, Panama, Mexico · WPRO/SEARO Break out o Philippines, Malaysia, Indonesia, Singapore	Facilitators: Country representatives
10:30-11:00	BREAK	
11:00-13:00	Presentations by groups Action plan **Comments/Recommendations for a CYD-TDV « test & vaccinate program strategy »**	Chairs: Annelies Wilder-Smith, Anna Durbin
13:00	DAY 3 – Lunch and Close	Duane Gubler, Annelies Wilder-Smith