Participants: Patricia Mouta (PM), Beatriz Lucchesi (BL), Beauty Moloto (BM), Beverley Cowper (BC), Chetanraj Bhamare (CB), Devang Patel (DP), Devi Sahoo (DS), Eliana Barros (EB), Gigal Soni (GS), Leticia Lignani (LL), Rajinder Suri (RS), Renata Pedro (RP), Shuyan Zuo (SZ), Katharina Hartmann (KH), Sonia Villaseñor (SV).

SV welcomed the participants and invited companies to present the advancements made in their own companies with regards to the AVSS project.

BL presented the project from **Instituto Butantan**. They are working in their prototype of Dengue attenuated vaccine that includes serotypes 1, 2, 3 and 4. The Butantan vaccine was formulated from an NIH liquid formulation. NIH performed the preclinical and phase I trials and then Butantan after developing the formulation, developed the Phase II trial with 300 participants, where the Butantan vaccine was compared with the NIH formulation and with placebo; it was to assess safety and immunogenicity with a 5 years follow-up study. Then Butantan started a Phase III trial in 17,000 participants 2:1 blinded with a placebo to assess safety and efficacy with 5 years follow up. It is intended to finish in 2024. Up to now, no important risks associated with the vaccine have been identified.
For dengue vaccines, participants are exposed to a theoretical risk of developing severe dengue after being infected by any of the wild virus if the immunity resulting from the vaccination is not balanced against the four stereotypes or if it decreases rapidly over a short period of time. Their objective is to perform an active hospital-based surveillance study to identify any severe warning signs indicating Dengue. They will also review the vaccination registry to verify if the individuals with severe dengue were previously vaccinated with Butantan vaccine. They will also characterize these cases in terms of duration of hospitalization and outcome. They will also compare the number of severe cases before and after the introduction of Butantan vaccine.

RS suggested this kind of study is quite risky when we are fighting for a dengue vaccine and it to be included in VIS; it could be more harmful. KH clarified that this kind of study is precisely what regulators are asking for. A similar study was performed with Takeda vaccine, and she congratulated Butantan on the concept they are doing. ANVISA is becoming an ICH country and will most likely follow what EMA and FDA are recommending. Antibody enhanced diseases is really a concern.

BL said that they have clarity that NRA needs to be involved. They are, however, struggling with the timing of the study, maybe one year or a longer period. KH thinks that it may be required to be made for a longer time.
EB added that Brazil has hospital epidemiology centers where they are responsible to notify cases that are of interest for the surveillance. They could work with this network in the whole country or maybe define certain regions or compare regions with the vaccine with regions without the vaccine. BL said this vaccine will be given to all population regardless their previous exposure to dengue or not; in their study they are identifying this background in participants. At this moment, results have shown that the vaccine is safe for dengue exposed and dengue-naive groups.

Biovac- BM and BC expressed that Biovac has been analyzing and listing the logistics of what needs to be done for the introduction of an MR vaccine into the EPI. The plan is that the new

MR vaccine is being included in the new EPI schedule for paediatric patients in 2024 however, they don't know anything about how the rollout will be done by the Department of Health in South Africa. It seems (but not confirmed) that there is not going to be a 'catch-up cohort' of adolescent and older women who haven't been vaccinated or exposed to rubella. They also do not have information on how the DoH/EPI is going to monitor the new MR vaccine introduction for future possible Congenital Rubella Syndrome cases.

A discussion around vaccination in pregnancy raised by KH. BC noted that there will be significant changes to the South African EPI effective January 2024 because of the introduction of new vaccines namely Tdap (to replace Td and for possible use in pregnancy to prevent early infant pertussis in line with the ROW policy), MR, PCV 10. KH asked if there is a plan to vaccinate pregnant women with Tdap and BC confirmed this is in relation to the Tdap new vaccine introduction situation. There are a number of vaccines being introduced to the EPI in 2024. One is Tdap for 6–12-year-olds replacing Td. as well as Tdap in pregnant women, PCV 10 (replacing PCV 13) as well as MR.

BC and BM outlined the progress that has been made on the MR proposal in terms of logistics and surveillance planning and KH said they have also made a good job with the information they have obtained so far. Once they have some more details about the MR rollout, they can adapt what they have already planned. Since they don't know the details of the MR rollout in South Africa in 2024, they are developing different theoretical scenarios which can be finalised or adapted in the future.

SZ from **CNBG** will present on the next meeting their advances.

RP and PM mentioned that **Bio-Manguinhos** has created their working group to work on Meningococcal ACWY vaccine. They are still in the phase of literature research about this vaccine, the methods that can be used, etc. In the next meeting they will be able to share more advances.

KH gave general feedback that companies are doing good brainstorming on what they need to do, and how, but they need more time. Our next call is on end-January. She made clear that we need to be very pragmatic and that we do not expect companies to deliver final synopses or protocols but the advances that were presented today are a good start because these are the things that they need to prepare before you get into the details of doing the study. So, she considers that the advances are successful.

Finally, BC asked the group if anybody has been involved in the rollout of a Rubella (or combination) vaccine into the EPI. RS suggested her to contact CB from SII, and BioE, as they are procuring high quantities of MR vaccine to UNICEF. SZ said that in China they used MR but now they use MMR. When they introduced this vaccine, they had many discussions on how to do the rollout. He offered to keep in touch via email to give more details.

Patrícia Mouta Nunes

Patricia Mouta
Chair - DCVMN PV WG