Attendees: Adriansjah Azhari (AA), Andrew Wong (AW), Marcos Freire (MF), Martin Reers (MR), Rajinder Suri (RS), Sandra Cho (SCh), Patrick Tippoo (PT), Apoorv Kumar (AK), Sonia Pagliusi (SP), Sonia Villasenor (SV), Tamires Lacerda (TL), Benoit Hayman (BH). **Excused:** Parag Nagarkar (PN). **Meeting started** at 12:01 CET and finished at 12:43CET

AA opened the meeting and welcomed the participants. He introduced Dr. Andrew Wong, who shared Walvax's experience with the development of different COVID-19 vaccine candidates in different platforms.

AW first gave an overview of Walvax company, which was founded 20 years ago and has 5 manufacturing sites; their R&D facility is based in Shanghai and in Kuming. Walvax has a portfolio of pneumococcal vaccines, HPV vaccines, Menincococcal vaccines, Hib and DTaP vaccines. AW also mentioned the vaccines on Walvax's pipeline, including COVID-19 vaccine candidates in which Walvax has made a great investment in development.

Walvax has developed COVID-19 vaccine candidates in mRNA platform, one for 1st Generation (for the original virus) and one 2nd Generation for a variant virus. Walvax has also worked in recombinant 1st and 2nd Generation vaccines. candidates. The mRNA 1st generation vaccine is targeted for 18 years old and above with a 2-dose regimen, 28 days apart. These vaccines are stable at normal cold chain 2-8°C and they currently have 9 months of stability data. 1 and 10 doses. They have finished phase III trials; in which they have included a booster dose, demonstrating that it is quite immunogenic and has a good booster effect. The approval of the vaccine is soon expected in China, and also the EUA as booster. The safety profile has been published in THE LANCET, showing that it is very similar to the licensed COVID-19 vaccines and induces a potent humoral and cellular immunity. It has also demonstrated that it could be a good booster for Adenovirus based vaccines. Walvax built a new manufacturing facility with modular technology in a record time of 10 months, which will have 400 million doses per year capacity, with a 3-phase project to expand capacity.

Walvax's mRNA variant vaccine is also targeted for 18 years old and above, to be stored at -15°C and below during 12 months or even from 2-8°C during 30 days. It is a 2-dose schedule, 28 days apart. The antigen used in this vaccine are Harvard and +Beta variant. Current data show they have a potent crossed protection event against Omicron.

Walvax' recombinant candidates project was supported by CEPI and with a 1M USD grant from BMGF. This vaccine is targeted for 18 years old and above, to be stored at 2-8°C tentatively for 24 months. It is also a 2-dose schedule, 28 days apart. The vaccine uses aluminum hydroxide + CpG dual adjuvants. Studies show it has a very good safety profile, immunogenicity and crossed protection against variants. The production site is under construction in Beijing and will be ready by Q4 2022 with single-dose capacity of 200-500 million doses/year. The prototype vaccine uses S-2P antigen and the variant vaccine uses S-6P (based on the Beta variant), which also increases the yield almost 12-fold.

AW shared a reflection on the lessons Walvax has learnt from COVID-19:

- The regulatory support would be key to license the variant vaccines, because it is not easy to find naive population for the trials of these vaccines.
- Sufficient funding from different sources was critical for the development of the vaccine at a rapid pace.
- Preferred technology platform that is both adaptable and scalable. mRNA technology is quite scalable and the investment is lower than the protein-based vaccines which require longer time and cost.

AW also shared some challenges and opportunities faced during COVID-19 vaccine development.

- Working with international organizations and technology partners is key to get a better antigen design and cross-reactivity.
- For the investment requirement for new technology, the support of Government subsidy and the grants from international organizations was critical, reducing the risk of investment of the corporations.
- On the policy side, the EUA will become fewer, so it will become a challenge to balance the regulatory requirements and to shorten the development time.
- On the packaging side, for mRNA vaccine the possibility to develop freeze-dried vaccine need a lot of studies and investment.
- Supplies of raw material and packaging materials are a challenge as some could be in shortage.

- On the regulatory side, since the mutation of the virus creates the need to develop new variant vaccines, the target population for clinical trial is shrinking. The regulatory system needs to be adapted, as it is a bottle neck to evaluate new technologies.

AA thanked AW and opened the floor for questions.
RS congratulated AW for the accomplishment made in a short span of time, also because Walvax developed an innovation on an innovation, being that the product is stable from 2 to 8°C. RS asked what was the need of Walvax of going for 2nd generation development while the 1st generation was still in the clinical development phase 3B. The variants that emerged before Omicron were really a concern and Walvax wanted to be better prepared. With the Omicron variant it is more about cross-protection for a good vaccine. It has also set the stage for multi-valent vaccines.

RS said that most mRNA vaccines are being questioned for their duration of protection, particularly even after 3rd and 4th boosters as immunity is not staying for long time. RS asked what are Walvax's studies indicating regarding the protection duration of their vaccine. AW said they are still collecting data on immune persistency for 3, 6 and 12 months, and are taking this into consideration as the need of a booster because of the lack of persistency is a problem. They are also aware that for mRNA vaccines, accessibility and cold chain are a problem mostly in LMICs; so their vaccine could offer an alternative to reach those markets that the current products cannot reach.

PT congratulated AW as it provides great encouragement to other DCVMs that great work can be done at scale in a short period of time. PT observed that Walvax is still rolling out its facility expansion project in anticipation of getting over 1.2 billion doses capacity, but there are some concerns expressed in terms of where the future of COVID might lead in the few years, he asked if AW is still convinced that this increase capacity should be taken to its logical conclusion. AW said that the phase 3 of the project could wait and see, but phase 2 will be completed. He considers that the mRNA technology platform is something that is going to stay. They have other mRNA vaccines being developed together with their partners and they need manufacturing capacity. He also considers that COVID will become seasonal, so there would be a market opportunity for booster vaccines. In addition, they have in development the 2nd generation variant vaccine which offers much better cross protection, so they need enough capacity planned.

PT then asked his view about the modular factory approach, is it that Walvax is looking to gear themselves to ensure a rapid expansion to other sites, or is it part of a strategy in terms of identifying technology transfer partners in other geographies in the world so that replication of Walvax's technology could be easier. PT also asked if their technology present challenges in terms of operating outside China and what is their strategy around that. AW said that the reason for using the modular technology was that they wanted to build up their capacity in a short period of time (10 months), but it is very expensive, it was a decision between time and cost, it was a special case. The high cost of a modular plant is an issue. For other kind production plants, he would suggest to go to the traditional way to build a plant. Regarding the freedom to operate outside of China, AW said they try to have their own IP, their production process and even some key ingredients. If they need something they do not have, they need to go to the original source and get some kind of arrangement, but for COVID is exceptional as some technology or information is free.

MR requested AW to confirm if the subunit vaccine they are working on is using a CpG-7909 adjuvant. AW confirmed so and said it comes from a Chinese manufacturer. He offered to give the contact details to MF.

AA asked if AW has plans to submit their vaccines for WHO EUL. AW said that for the mRNA they will submit for EUL to reach more market, and also for the subunit vaccine, it is a requirement from CEPI to apply for EUL.

AW added Walvax is open to all kinds of partnerships from full tech transfer, bulk export or just distribution.
AA thanked AW and closed the meeting.
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Notes taken by SV

Adriansjah Azhari
Chair DCVMN COVID-19 Committee, April 14th, 2022