Attendees: Adriansjah Azhari (AA), Bernadette Hendrickx (BeH), Hong Thai Pham (HTP), Katharina Hartmann (KH), Laura Viviani (LV), Marcos Freire (MF) (left early), Martin Reers (MR), Nishant Vora (NV), Rajinder Suri (RS), Sandra Cho (SC), Parag Nagarkar (PN), Sameer Naik (SN), Sivashen Cunden (SC), Sonia Pagliusi (SP), Sonia Villasenor (SV), Tamires Lacerda (TL)

DCVMN COVID-19 Committee at 12.00 CET and finished at 13:06CET

AA chaired the meeting and welcomed the participants. AA introduced Dr. Parag Nagarkar as Co-chair of the COVID committee (Head of Global Regulatory Affairs at SSIL) and Dr. Sandra Cho as Secretary (Regulatory Affairs Manager of Instituto Butantan), who then introduced themselves.

PN then introduced Dr. Sameer Naik (lead of the COVID19 QC team). SN gave a presentation on understanding COVID-19 vaccines challenges ahead. SN recognized that COVID-19 pandemic has made the development and licensure of vaccines extremely quickly compared to the regular timeframe to develop vaccines. High financial support as well as private-public consortia have been of a great support. Several technologies have been used/developed for new COVID-19 vaccines. A major challenge is the production and distribution of the vaccines.

SN mentioned different platforms that have been used for developing COVID-19 vaccines and mentioned some of the manufacturers using each of them.

- **mRNA-based vaccines**- Was the first one of this type. Developed by Pfizer and Moderna.
- **Viral vector vaccines**- Developed by Astra Zeneca and Oxford university and in association with SIIL; using a chimpanzee adenovirus with its gene deleted and inserting a gene to replicate the spike protein of the Wuhan COVID-19 virus. Similar approach was used by Gamaleya institute using human adenoviruses.
- **Subunit vaccines.** Made by expressing the spike protein in a papillovirus expression system and obtaining the purified ~~the~~ spike protein.
- **Live attenuated virus vaccine.** Many traditional vaccines are made using this platform; however, it takes years to make a live attenuated vaccine, however this can be made using the modern genomic approaches. SIIL is working with this technology having 1000 cuts in the genome.
- **Inactivated vaccines**. Used by Bharat, Sinovac.
- **DNA based vaccines**. Used by SANOFI and INOVIO

The identified challenges associated to the COVID-19 vaccines were:

1. **Scientific.** Th first challenge found when the COVID-19 pandemic emerged was the unknown epidemiology of the SARSCoV-2 Coronavirus, and then the different mutations and generations of variants. Variants cause variability in the severity and symptoms of the disease. This has been little by little ~~been~~ published thanks to the work of scientists and healthcare workers. Also to select and/or develop the most suitable platform to develop efficacious vaccines. Now that vaccines are available, how long will the immunity last in the vaccinated individuals and/or recovered patients. The challenges remain as to increase the stability of the vaccines to facilitate distribution.
2. **Technological.** Vaccines were developed in different new platforms like DNA, mRNA, and others already mentioned. The challenges faced and still being faced are the supply of raw material and manufacturing consumables, packaging material, etc. The characterization of the seed and substrate is very time consuming. Many laboratories that offer these services are not available in DC. Scale up of manufacturing is a big challenge to get to large manufacturing capacities. Analytical development, validations and stability studies are also a challenge due to the limited knowledge of the stability of the vaccine and its possible shelf life and storage. These were satisfactorily predicted by using statistical modeling.
3. **Clinical and Regulatory.** The current challenges being faced to the future by the new vaccines developers as well as by the developers of new variant vaccines are the recruitment of healthy, naïve volunteers for the clinical trials of the vaccines and then doing the follow-ups and analysis of the data. Obtaining the regulatory authorization for R&D, manufacturing, clinical trials and stockpile was a challenge, however, many regulatory agencies applied fast-tracking procedures for the vaccine evaluation and approval. An important factor is to complete the transfer

method and training of national control laboratories for the timely completion of testing and release of COVID-19 vaccine batches.

4. **Barriers for the local production.** Different vaccines have been developed by several corporate entities, laboratories, etc. and an important constraint in the scaling up of access to vaccines in developing countries is the intellectual property rights (IPRs) and the willingness to share technological knowledge, expertise and know how during the technology transfer is critical for the success of the technology transfer. Export restrictions of the vaccines as well as tariffs established by the governments are also a challenge faced. Likewise, the partnership model and licenses for technology implementations, are also a challenge for the different types of partnerships. Intellectual property rights, regulatory rights and others had also to be solved. In spite of these challenges many companies have successfully sorted them out.
5. **COST.** It is perhaps the most important part. The major contributor of the cost is the cost and uninterrupted supply of raw material. An important point highlighted is that some companies have set lower prices for the vaccines for developing or the poorer countries despite the investments made for capacity building, as well as to the volume of vaccines that need to be manufactured to cope with the need of the nation. Despite all those facts, some of the manufacturers have committed to set the lowest possible prices. Another factor that has been contributing to the cost of the vaccine is the vaccine wastage due to different reasons.
6. **Availability and distribution.** This factor is very related to the cost of the vaccine. Once the vaccine is available in the market, some countries have purchased or signed for a high proportion of the available vaccine doses from the manufacturers, leaving other countries without the needed vaccines for their population. Other challenges are related to the storage facilities and proper transportation of the vaccines at subzero temperatures. Vaccines for young adults and toddlers are still not available, although in development. An important challenge is also the counterfeit of COVID-19 vaccines being reported in several countries.
7. **Social.** Vaccine manufacturers are facing vaccine mis-trust that has been spread in social media by several groups of people who think the vaccine is unsafe or it is not the solution for the pandemic. This has been created by bio-hackers (doing yourself-biology) who have created different videos or forums that pretend to instigate the potential vaccines by generating fear on the possible (documented or undocumented) secondary effects. Booster doses campaigns are also a challenge on one side for ensuring the availability of the vaccine, and on the other about the policy makers are not yet in agreement.
8. **The unknowns.** These are vital questions we need to make at this point. Who will be protected from the COVID-19 infections post vaccinations? We need to understand the longevity of immune responses, the role of adjuvant and to extend the protective immune responses post vaccination. What about vaccines for children, pregnant women, and high-risk groups? We need to understand about the long-term efficacy of the vaccine and its possible side effects. And also to understand and overcome the financial and political problems and to allow the COVID-19 vaccines be made available with equity around the words.

The future goal is to design vaccines against variants, develop multivalent vaccines and to obtain higher antibody titers by defining the re-vaccination schedules and or developing/modifying the vaccines.

SP asked about how the counterfeit vaccines were detected and why they got into the market, and what to do in order to prevent it. SN said SIIL faced some cases of counterfeited vaccines in the market. They made certain changes in the primary package with unique design helping prevent counterfeit as they are difficult to replicate. For secondary packaging SIIL has introduced several security features to distinguish from counterfeited drugs.

AA presented then a slide on the suggested topics for the coming 6 months for the COVID committee and requested for inputs from the team:

Quarter	Suggested topics	Presenter
1	Understanding COVID-19 vaccines - Challenges ahead - New variant related changes	Dr. Sameer Naik (SIIL)
	Strategies on booster immunization	

	Discussions on drafting proposition papers	
2	COVID-19 vaccines for children	
	Pharmacovigilance & RMP for COVID-19 vaccines	
	Follow up discussions on position papers	

AA requested COVID committee members to send their suggestions on the topics for position papers or discussions by email.

AA reported on a meeting with CEPI who initiated the implementation of CMC platform protocol templates for comparability and PV/PPQ so that it could be a guidance for future prospect vaccines. This project is targeted to start in Q1 2022 and finished in Q4 2024. CEPI has established two working groups, one would be focused on drafting the templates on comparability and the other one process validation. DCVMN is expected to nominate 2 representatives, one to join each of the working groups. We can also propose which are the platforms we prefer to work on.

PN proposed himself for both working groups. SP mentioned that perhaps MF would be interested in participating in one of the groups, but AA would need to ask him since he had left the meeting early. SP suggested for all DCVMN members participating in meetings with CEPI, WHO and others, to report this group on the advances and initiatives. AA will follow up on one representative who has been joining in the scientific group and one in the clinical trials.

RS suggested to identify in advance the speakers for the next topics to be covered. He also suggested to look for ways to increase the level of participation of the members in the committee.

AA thanked the participants and closed the meeting.

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Notes taken by SV

Adriansjah Azhari
Chair DCVMN COVID-19 Committee,
February 10th, 2022