Attendees: Abdulaziz Almutairi (AA), Venkataraman Hariharan (VH), Shubanghi Gadge (SG), Sebastian Comellas (SC), Wendy Huang (WH), Monique Stavale (MS), Samir Desai (SD), Mic McGoldrick (MM), Jacqueline Dias (JD), Ana Basso (AB), Nora Dellepiane (ND), Sonia Pagliusi (SP), Laura Viviani (LV), Sivashen Cunden (SC), Tana McCauley (TM) minutes

ND started the meeting at 12:11 by welcoming the participants.

I) Updates

1. Status of activities with WHO: COVID vaccines registration, PACs GL revision, PACs within CRP. MM briefed the WG on COVID vaccine registration earlier this month. MM added that the letter on WHO PAC guidelines was sent to WHO. MM is also putting together a letter regarding COVID vaccines and registration pathways. MM will send out the final version of the letter shortly. DCVMN will be able to sign the letter.
2. ICMRA letter. The ICRMA letter was circulated to the WG as a pre-reading. It put forward recommendations to support the rapid increase of COVID vaccines production and capacity changes (ex: the need for filling lines/sites). The letter asks for facilitation of these variations.

II) Briefings

1. Status of regulatory alignment on 3Rs implementation. LV briefed the WG on regulatory alignment on 3Rs implementation so that DCVMN members are up to date on changes related to obsolete animal testing or 3Rs opportunities. Critical issues with animal testing include the cost and need for repeated tests. One of the hurdles is the lack of regulatory alignment, with different testing requirements from different regulators. Some key ongoing global projects are the HSI deletion or waiving of ATT, the NC3Rs and WHO collaboration to review animal use requirements in the WHO biologics guidelines, and the DCVMN PSPT Project to replace the intracerebral-challenge by a serological assay for wP vaccines. ND opened the floor for comments and questions. SG shared her experience regarding the ATT, which they succeeded in deleting in India and most countries. However, some countries insist that the ATT should be conducted. SG will use the publications and try to convince these countries. MM asked about the countries that request ATT. In his experience, it was Russia, Korea and China. SG replied that Mexico, Vietnam and Turkey requested the ATT. MM explained that by providing PV surveillance data in Mexico, the regulator could waive the ATT. In Russia, it is possible to perform the ATT for one out of 3 or 5 batches, and Korea is considering the test's deletion. These efforts have been slowed down because of COVID. If the ATT is still required in the pharmacopoeia, if you provide PV surveillance or production consistency data, the regulators may consider waiving the ATT. WH shared the example of China where the Chinese NRA rejected requests to perform in vitro potency testing for HPV. Now they are testing in parallel using in vivo and in vitro tests and collecting the data. However, the timing is hard to predict, and it is not sure how many batches they will request to be able to use in vitro potency testing only. LV added that parallel testing is effective and has worked to convince NRAs in other countries. SD added that once the required data and justification have been provided, there shouldn't need be any repeat test. ND noticed that progress had been made, albeit slowly. It is worth trying, with PMS data and formal request for a waiver or deletion of a test. MM explained that part of the additional information that goes in is compliance with GMPs and counteracting the whole point of doing ATT. **ACTION:** TM to share LV's presentations and the list of publications to the WG. LV circulated the 3Rs slides presented to the DCVMN regulatory on 22nd March, which were circulated to the group on 24th March.

2. Work plan. ND went over the 2021 work plan. Key updates included: following up with WHO to foster increased CRP implementation, fostering PACs management improvement through the participation of DCVMs in CEPI workshop and the collaboration with IFPMA in asking WHO for revision of the PACs guidelines for vaccines. 2021 activities involve moving forward with CRP implementation (letter sent to WHO but waiting for a response) by doubling the number of countries adopting CRP (16) and increasing the manufacturers registering vaccines through CRP. Other activities include improving PACs management for CRP registered vaccines by collecting manufacturers' experiences with CRP registered vaccines in the relevant countries and sharing them with the WHO CRP team. Another activity is to strengthen the capacity that DCVMN members have in RMP, which is essential for the registration of COVID vaccines.

3. Progress of RMP Project. ND briefly presented the project. The project's outcome is to strengthen the capacity of DCVMs for the development of risk management plans for vaccine registration and PQ submissions to meet the ICH

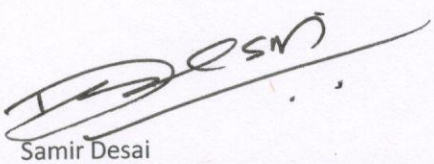
guideline E2E part (cf. https://www.ich.org/page/efficacy-guidelines) and EMA GVP GL. The expectations are that manufacturers will establish a company multidisciplinary team for RMP plans and prepare an RMP that meets the EU standards and can be integrated into the CTD. Manufacturers can then submit the vaccine chosen for the project for registration/WHO PQ.

4. Data collection on PACs management within CRP and FU to PACs publication. ND asked the WG for their opinions on moving forward with PACs, and if companies had faced any problems on reporting variations through the CRP process. VH answered that it is too early for BBIL, and they had not encountered any situation with variations. They had directly submitted to countries and who had engaged with them. SD asked the WG if there were to be challenges encountered, how would the WG ensure WHO gets the information. VH answered that BBIL is open to sharing with WHO, but details on sharing data should be decided within companies. SD replied that these experiences are company-specific, and nobody apart company and regulator will be aware of this. ND explained that when you use CRP for registration, the second step is about how the variations should be managed. The idea is to keep the product the same. If you submit the variations out of CRP procedure, the information on these products changes. In that case, and the CRP is not useful anymore. What is submitted to WHO then has to go to countries, which should almost approve immediately. When the CRP process reaches the stage of management of variations, problems have previously arisen regarding drugs. CRP for vaccines has just started now. That is the reason why WHO wants to know if this is going smoothly. SG shared her experience with CRP. Acceptance through CRP is a challenge. Countries are willing to accept vaccines through CRP, but they are not specific and precise about the variation system. With the CRP process, health authorities rely on the WHO PQ VAR system, where they keep information and changes. There will not be required variations with health authorities, and will send variations to PQ VAR systems. SG noted that they will share their challenges with WHO. ND recommended staying within WHO processes. Variations management should be managed in the same systems. We can try to see the problems with this and collect data. **ACTION**: Establish a task force between manufacturers that have already registered vaccines using the CRP to follow up on the process for communicating (and approving) variations to/ in relevant countries and capture any issues that may come up and share these with WHO.

5. TORs revision. ND asked the WG for their comments regarding revising the TORs and seeing if the chair and co-chair would like to renew their positions. ND suggested giving the WG a week to go through TORs and suggest any changes. The WG may also have a short meeting to discuss and elect a new chair and co-chair. **ACTION:** Circulate TORs until Monday 29 March asking for points to be revised and also asking for volunteers to Chair and/or Co-chair the committee. **ACTION 2**: Circulate invitation, asking for interest and WG members' availability to become chair and co-chair.

6. AOB. SP said she received an invitation on regulatory approaches to PACs on COVID vaccines. MM put together a Regulatory Advisory Group (RAG) pre-read for questions. The document will then be submitted and discussed by RAG, then sent back to MM. SP noted that there are no DCVMN members in the RAG. **ACTION:** MM to share with the RWG the document to be discussed at the SWAT reg meeting on dealing with COVID 19 variants. Consider the need to have a DCVMN representative in this SWAT group. MM shared the DRAFT document from the IFPMA industry group, (supporting COVAX SWAT on PACs) with DCVMN secretariat on March 22nd, which was circulated on the same day to the DCVMN regulatory group members for comments, and a reminder circulated on the 23rd March.

ND closed the meeting at 13:37 by thanking all the participants.



Samir Desai
Chair of the Regulatory Working Group
March 22nd, 2021