Attendees: Ida Nurnaeni (IN), Venkataraman Hariharan (VH), Kumar Gaurav (KG), Meenu Jain (MJ), Shiubanghi Gadge (SG), Nirav Chokshi (NC), Sebastian Comellas (SC), Wendy Huang (WH), Norbert de Clerq (NC), Mic McGoldrick (MM), Lorenz Scheppler (LS), Paula Barbosa (PB), Nora Dellepiane (ND), Sonia Pagliusi (SP), Laura Viviani (LV), Tana McCauley (TM)

ND started the meeting at 12:08 by welcoming the participants.

Presentations on CRP Implementation. ND shared SG's presentation on SIIPL's CRP experience for a pneumococcal vaccine in Malaysia. Registration dossier in ACTD format was submitted to the National Pharmaceutical Regulatory Agency (NPRA) Malaysia in September 2019. The product was granted WHO PQ in December 2019. Due to the urgency of registration, NPRA suggested proceeding with WHO CRP in January 2020. Registration documents required for CRP were submitted. Some country-specific administrative data was needed for Module 1, and a bridging study for vaccine suitability in the Malaysian population was requested. Queries on clinical trials, PV data, PV reports, SLPs, and batch release certificates for 3 batches of different product strengths were responded to. Registration was granted in July 2020 (after around 6 months). Approval received was with a validity of 2 years and is a conditional approval. One of the conditions is "upon product renewal (after 2 years), evidence of satisfactory GMP certification by NPRA or by any PIC/S participating authority to be submitted". Registration approval timeline is almost in compliance with the timelines stated on WHO website for CRP process. The variation filing process is ongoing.
ND presented Biological E's experience with CRP. BE initiated the registration process of PQed vaccines in May 2020 using CRP. BE targeted registration for one of its PQed vaccine in 17 countries. So far, BE obtained product registration from 5 countries (Zambia, Ghana, Sierra Leone, Malawi & Tanzania) within timelines. BE has not yet faced any situation for handling variations. BE identified the following hurdles in the process: 1) Not all NRAs are fully aware of CRP process and its implementation for PQed Vaccines. 2) NRA can reject the Expression of Interest (EOI) for CRP procedure 3) No explicit provision is mentioned converting the existing national registration process to CRP, which would be useful for accelerating the approval process. 4) NRA requires a full dossier even though the vaccine is PQed. Still, manufacturers need to submit product samples, even though the vaccine is Prequalified after testing by WHO-approved laboratory as part of PQ process. 5) Manufacturers still need to submit the variations post-approval though it followed WHO variation guidelines for intimation of variations, which significantly increases the burden of life cycle management. BE has the following recommendations for improvement: 1) Manufacturers should only request submission of an abbreviated dossier containing the summaries of CMC, Non-Clinical and Clinical studies to NRA to grant registration for a PQed vaccine. 2) It would be great if submission of variations is waived-off, as all PQed vaccines follow WHO variation guidelines, OR the variation guidelines shall be clear and easily accessible to NRAs. 3) NRAs should accept vaccine registrations for all PQed vaccines, as it is currently being applied for only specific vaccines.ND commented BE's presentation. The CRP dossier submitted to countries, and WHO PQ is usually the same but countries still have the right to require a different one. The push in the future would be to use the same dossier as WHO PQ. The submission of variations is something that WHO is dealing with now.

VH presented Bharat's experience with CRP. They submitted for CRP in 30 countries and could successfully register in 3 countries (Zambia, Nigeria, Botswana?). The process took place within 90 days. However, there were some issues in other countries, where the process took longer. Whenever there is a country query, the clock stops, and the process can take more than 90 days. There were some delays in Zimbabwe and Botswana, where the PQ team could not connect to the regulatory team. The process took 2-3 months longer. In Zimbabwe, there was a situation where the CRP team found that Bharat had not submitted the dossier; however, the CRP team was in contact with the wrong entity. Some delays also occurred when the administrative documents were shared with the drug administration. The 90 days expired, and they contacted the CRP team and received a query from the country. This was regarding filled documents that manufacturers do not typically share as part of the registration dossier. Bharat informed the country they could share the documents on-site. The issue was resolved during the virtual audit. As BBIL could share the required executed documents during the online Audit.
ND opened the floor to comments on the presentations. The WG had no further comments. **ACTION: Summarize the experiences with CRP and share with WHO during the next meeting to discuss CRP**

Updates: Recent Activities. ND shared information about two recent meetings DCVMN and IFPMA attended: WHO 8TH Annual Meeting on CRP and the UNICEF-UNFPA-WHO meeting. The WHO annual meeting on CRP focused on managing variations within the use of the CRP procedure. It was mostly related to medicinal products, which are at a

stage where they are facing problems with the reporting of variations. WHO aims to make the management of variations easier. ND committed that DCVMN would collect data and focus on reporting variations to see how it will go. The plan is to share the findings with WHO. However, the main concern now is trying to increase CRP implementation in more countries, for more vaccines, and inviting WHO to provide more resources to PQ team, as the PQ now is engaged on COVID and do not have as much time to work on CRP. During the UNICEF-UNFPA-WHO meeting, there were sessions on access to COVID health products updates on WHO and UNFPA PQ programs, CRP overview, WHO regulatory updates, local production, and procurement. DCVMN commented and endorsed WHO efforts on facilitating the implementation of EUL for COVID vaccines and the WHO approach to improve access, for countries to accept the EUL without more work on it (if there is a need for more work in certain regions, regional experts can be involved).

Current and Future Priorities. ND presented the WG priorities for 2021 and invited all members of the WG to participate in the discussion.
ND shared the summary of the work accomplished in 2020: PACs paper published, Push for CRP implementation (9 V, 6 M, 8 C + 1 CARICOM), Group discussion on the WHO document on considerations for eligibility for EUL pathway for COVID vaccines, Comments shared with WHO and taken into consideration on WHO final version, e Workshop on CTD including a briefing on eCTD

- Development of the document to guide manufacturers for CRP implementation and to be published on the DCVMN website (password-protected). VOTE: Agreed 4/5
- The WG members will go through and give their comments on the IFPMA-DCVMN joint letter to WHO to request a revision of variations guidelines by 6th January 2021.

The WG voted on future priority activities:

- Continue to push for CRP implementation. VOTE: Agreed 4/5
- Collect manufacturers' experience with variations management in CRP context. VOTE: Agreed 4/5
- Strategy on how to move forward with the recommendations on PACs management. ND asked if this would be a priority for DCVMN and IPFMA. MM suggested scheduling this topic as the main agenda item in Q1. VOTE: Agreed
- Timely review and feedback on WHO draft guidelines published for comments. ND suggested that someone in DCVMN Secretariat monitor the WHO website to check for any relevant documents to be commented on/discussed. VOTE: Agreed 3/5
- Decisions about meeting with WHO on CRP or to focus on variations as the primary collaboration with WHO. There was a discussion during the previous WG meeting to send a letter to WHO to set up a meeting on CRP. SP suggested meeting with the WHO to discuss CRP's shortcomings, despite the WHO now being busy with COVID. SP also recommended asking the companies with experience with CRP if they would like a meeting with the WHO. VH and SG agreed that it would be a good idea. SP noted that the meeting could be open to IFPMA and others, as CRP is for all manufacturers. VOTE: Agreed.
- DCVMN identified some training needs: eCTD, risk management plans, and statistical analysis of stability data. SP updated the WG that the pharmacovigilance WG will give training on risk management planning and benefit/risk analysis. The Regulatory WG will focus on training for eCTD and statistical analysis of stability data in 2021. VOTE: Agreed
- Specific Regulatory WG project. SP asked the WG if they had any ideas for a project. SP briefly presented the 3Rs WG PSPT project. SP gave as an example for the WG to work on eCTD implementation. Project participants can exchange information (non-confidential) and share successes/difficulties. DCVMN could provide resources like consultants, software, information... ND suggested giving the WG members time to think and come up with proposals.

ND closed the meeting at 13:48 by thanking all the participants.

Ida Nurnaeni
Co-Chair of the Regulatory Working Group
December 17th, 2020