Participants: Sebastian Comellas (SC)-Sinergium, Wu Cong (WC)-CNBG, Monique Cruz (MC)- Bio-Manguinhos, Subhodeep Chakraborty (SCh)-Zydus, AbdulAziz Hamid Almutairi (Arabio), Pieter Neels (External consultant), Sonia Villaseñor (SV)-DCVMN. **Meeting started at 12:05 pm CET and adjourned at 12:45 pm CET.**

SC announced to the group that we have a new external consultant Dr. Pieter Neels.

1. SC mentioned that since the group has decided that post- approval changes (PAC) is a priority topic for the WG,
   a) SC has been working on a draft of the Moodle course regarding PACs, with the following sections:
      - WHO TRS 993 Annex 4 "Guidelines on procedures and date requirements for changes to approved vaccines"
      - Main challenges experienced by manufacturers with PAC in developing countries (Reference to paper published in Vaccine (August 2020)

   b) What can be done in the future to improve PACs management
      - Changes proposed to the WHO by IFPMA and DCVMN

   c) What are the possible solutions or approaches that can be considered

   d) Closing remarks (proposal to improve the situation)

SC will polish the presentation and I will share it during the weekend with the WG so that in function of the experience in different countries or regions, make modification and add information to improve the training. The members of the WG are expected to give their feedback in 2 or 3 weeks. SV suggested to have around 100 slides so the draft will need much inputs and commitment from all the participants.

2. Approaches for improving situation. SC mentioned that the situation in Latam is similar nowadays with respect to the situation in 2019 when the WG performed the evaluation. There is a clear lack of harmonization because every NRA has different criteria on PAC. One strategy is to request a meeting to PAHO to explain the situation to understand if we can work together to improve the situation in Latam.

Other strategies are needed and requested the feedback from the group. In the last meeting SC proposed is that changes should be approved in the country where the vaccine is manufactured, and ideally no additional evaluation when the product is imported into another country. However, this is not easy to implement because each NRA wants to perform their own evaluation so it is important to foster reliance concept.

MC suggested to leave time for the team to think and propose strategies by email. SC appealed the WG members to work in between meetings, otherwise no results will be reached.
SCh mentioned that in the last meeting there was a suggestion for harmonization of guidelines. Once the language of variation is uniform across, then only it would be possible to evaluate this strategy to be approved by NRAs and the go to different countries' regulators and approach for their acceptability. The challenge here is that when we look into the classification, if something which is not published in their variation guideline, but which is there in some other countries or WHO guidelines. So, then it will it becomes very tricky to convince on the class of variations. On this point Mic McGoldrick (MM) has also commented during the previous meeting that there is a work which is going on to actually harmonize this. SCh then proposed that the strategy should be first to bring everything in a platform, and let it categorize in a globally harmonized way, and then

we can think of reliance across different regulators.
SC agreed, but still suggested that to move forward we need to be in communication with a stakeholder. MM had mentioned that for WHO this topic is not a priority, so SC is suggested that DCVMN & IFPMA could propose together to WHO some important topics that should be updated regarding WHO TRS 993 Annex 4. This needs a deeper discussion with IFPMA to go together. SC will approach MM to discuss on different strategies to work together; if IFPMA does not consider it as a priority, we could approach PAHO, if Mr. Suri agrees.
SCh will also check with his internal team about their approach and interest. We need to focus on reliance and convince our NRA either by pointing the gaps with WHO guidelines or we can highlight if there should be some more clarity in terms of variation filing. Breach those gaps would be a good step. There would be a lot of challenges in this, so collaboration is required. SCh will write an email about the strategies or about the condition with the NRA in India and we can carry on from there.

3. PN introduced himself and his vast experience in regulatory from the side of regulators, industry and academia.

SC requested PN suggestions of topics useful for manufacturers for the WG to work on in 2024, after finishing the project on PACs.
PN mentioned that the BMGF is willing to finance meetings on Next Generation Sequencing (NGS), a new technique to detect adventitious agents in vaccines; the US FDA is keen on this technique, because it is simple, quick, cheap and doesn't need killing mice. A webinar was given in DCVMN last year but we could go deeper to replace many other testing techniques.
Other topic is real world evidence, which could be used in combination with challenge trials. A conference with African regulators, in collaboration with EMEA and FDA was made recently to discuss if they are willing to make challenge trials in Africa and if they would be willing to accept the data coming from these challenge trials in order to replace field trials. It could be convenient for a number of diseases to combine challenge studies and real-world evidence. So, this could be an interest topic to look at. SC agreed this could make the products get faster into the market. He mentioned that some manufacturers need support to evaluate clinical trials from a regulatory point of view, and a training could be developed for manufacturers to increase their knowledge in this topic. PN said he is willing to work on this. The members expressed their interest in this topic.
He suggested also to pay for a good medical writer and publish the report, which he does for the activities he is involved in.

SC said that a workshop for the WG would be very useful to improve the knowledge of the manufacturers in regulatory topic. He asked the members to think about the topic they would like the workshop to be about. SV announced that the dates are authorized to be **24 and 25 November** in Singapore, so only the topic needs to be defined. Some suggestions he gave was about the differences between CTD format around the world, but the WG has already worked about this topic in the past. SC will contact the group to define this.

SC suggested that on the last WG meeting scheduled for December, the group can define the topics to work in 2024. These could be reliance. He also emphasized that the members need to work between meetings in order to get results.

Sebastian Comellas
Chair of the Regulatory WG

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