PSPT steering group meeting

September 1st, 2020

Attendees:

Christina Von Hunolstein (CV), Arjen Sloots, (AS), Coenraad (Hendriksen (CH), Irma Riyanti (IR), Pavlinka Stoyanova (PS), Stan Deming (SD), Sunil Gairola (SG), Ute Rosskopf (UR), Laura Viviani (LV), Sonia Pagliusi (SP), Sonia Villasenor (SV) minutes.

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1. The meeting started with an **introductory roundtable** of all the PSPT steering group and the observers.
2. **Intravacc's role(s) in the Consortium**. LV and SP explained that Intravacc is a DCVMN resource member, DCVMN never has any transaction with any member or resource member. In this specific project we did receive a waiver from the DCVMN Executive Committee in order to establish a specific service agreement with Intravacc, as it will be paid with awarded grant for characterizing the coating antigen; at the same time Intravacc also expressed an interest of being part of the steering committee, and to be a member of the consortium. Thus, the secretariat asked for advice of the group to avoid raising potential conflict of interests now or later with the DCVMN members involved or not in the project.
   It was confirmed and highlighted that Intravacc's representative, AS, participating in the steering group is from a different department unit from the one that will provide the service.
   It was agreed that in case of any decision of the group that is directly concerning Intravacc's role, Intravacc should excuse from providing an opinion, or whenever Intravacc, or in general any member of the Steering Group feels that the issue is too sensitive or has any potential conflict of interest, the member is going to excuse him/herself from the voting process, but still can be part of the scientific steering group and discuss and join the decisions on other topics. The minutes of the steering group will be available only to DCVMN members, distributed to the others participating laboratories, and shared on the PSPT Consortium website.
3. **Approval of Steering group roles.** LV presented the proposed roles of the PSPT steering group, and all roles have been approved by the group. The Steering group will meet every quarter; or in case there is anything urgent or important to discuss it can have ad hoc meetings. Materials to be discussed will be distributed 2 weeks earlier. Members can vote, observers do not have the right to vote. Decisions will be made by the majority of the votes. CV is the casting vote in case of tie.
4. **Status of the project**. LV reviewed the deliverables expected for the project. She presented the quote from CMO, which is going to be finalized and signed soon, with minor technical changes. The quotation was approved. CV asked if the protocol was checked with Intravacc. LV and AS said that they discussed several versions of the quote, contract conditions and inactivation procedures. In particular, CMO would come up with several different inactivated and lyophilized samples, and after that, Intravacc will test and see which will be the best. They will compare the new coat by testing it with positive anti bordetella sera from the previous study (ECVAM or BSP104).
   A specific discussion focused on some technical aspects of the coating antigen production:
   - Synthetic media - AS explained this was a media developed by Intravacc many years ago. It is better to use a chemically obtained media rather than the ones used before. The development of the synthetic media has no relation with the PSPT Project.
   - Use of formaldehyde for inactivation and validation of the inactivation process. AS said that they don't think Intravacc can validate that because they are far apart from the CMO, and the CMO will test for the inactivation of bacteria as part of their QC testing. They will test on agar plates to see if there are live bacteria. CV, as well as SG, are concerned of the impact formaldehyde will have on the coating antigen preparation, because previously they didn't use formaldehyde to inactivate the bacterium. CH confirmed that they used only inactivation at 56°. AS reviewed the inactivation conditions of the 7 samples and there are some of them using formaldehyde in the inactivation, others just inactivation at 56°; at least one of the seven conditions should be similar to what was used in the previous PSPT validation studies. To be discussed is the concentration and production of casamino acids. The idea is to use the conditions that were used in the previous PSPT studies, that will be one of the 7 samples. AS said that they plan to use LC-MS, but not to test the engineering run; the antigen coat preparation needs to be tested in the whole cell ELISA.
   - SG suggested also to test the liquid formulation in ELISA before lyophilization as a control to see if there is a change in LC-MS after lyophilization, as a backup; he is concerned whether LC-MS is really giving an indication of the quality of the product. Because if you do only a heat inactivation, only the physical state of the bacteria is altered. Adding formaldehyde, a lot of things can change the proteins. If we succeed with one of the 7 samples, and do the inactivation without modifying the material chemically it will be very good for ELISA. SP asked if it would be necessary to ask the CMO to include this in the contract. AS responded that it is not necessary as it is already considered in one of the 7 samples. In case they behave

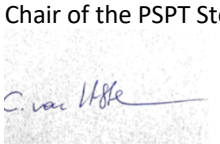
equally and one is containing formaldehyde and one is not, we would prefer the one that does not contain formaldehyde.

- CV asked if there will be a test *in vivo* to qualify the bacterial virulence obtained by fermentation; AS answered it was done in the previous study as they wanted to produce coating antigen and at the same time producing *B. pertussis* 18323 for performing the Kendrick test to be sure that the bacteria grown were virulent. However, this is not relevant for this project, as it will cost a lot of animals, and there is no sense to perform a virulence test. It is easy to see in the Bordet Gengou Agar plates if the bacteria are in virulent state because they lyse the blood on the plates and a halo will appear.

The CMO quote was approved and any additional technical questions will be sent by email to LV and she will circulate to all the final quote.

5. **Discussion on the in-house validation study design**. The commitment originally with the participating laboratories is to perform the Kendrick Test (within the routing testing activities) and PSPT with a minimum of 3 batches plus an altered one (Kendrick not routine). CV mainly asked who will be preparing the SOPs for the PSPT, assuming each laboratory has their own Kendrick SOP.
   CV said we need to prepare SOPs for immunization of animals, bleeding and ELISA. CV and CH volunteered for this task. Regarding the Kendrick test, she requested LV to distribute the answers of the survey regarding the use of animals. LV said she will distribute it to the steering group although not many details were gotten from it.
   SP said the 3 batches +1 altered is the minimum every consortium member should be conducting, if the labs would like to test more batches are free to do so.
   UR asked that if the manufacturer will be testing batches with PSPT that will be releasing commercially so they will have the Kendrick test for all of these batches. The question is they use the regional reference and maybe they can perform the PSPT test also on that. LV confirmed, based on the survey that the majority of the labs are using regional references. CV said that it was discussed very early that if labs use currently a regional reference, they are invited to test also this in PSPT. It can be used to estimate the vaccine potency in comparison to the in- house reference, or detect relevant differences in assaying the regional reference immune response among labs.
   SP suggested that the study design should be drafted as presentation, and it needs to be clear and then presented to the consortium members, maybe not in the kickoff meeting, but later. The presenter should be in a position to explain everything clearly and maybe we can find a presenter to communicate this to the participants, maybe UR. The design must be clear to avoid misunderstandings. SD added that it should be clear what is going to be validated, and also which are the validation criteria, and how a lab will know to have achieved validation. That should be in the presentation. CH suggested that since CV and Intravacc had been involved in previous studies, they could together do the writing SOP and narrative; he volunteered on behalf of Intravacc. CV agreed. She said that since the study design was already indicated in proposal of the project, they have only to make a description narrative of what we want from the participants of the project; not put on discussion the study design.
   SP said that 3 NCLs and one manufacturer who is not member of DCVMN joined the project, but did not follow all the discussions we had before. SG clarified that the study design is the first one that gives a broader idea, then SOP will specify the use of reference material, the exact way to perform assays. Since it is an in-house validation study, the variability will be very high depending on the manufacturers' positive and negative controls they are using. So, the SOP must be debated first, before the formal kickoff meeting. This was agreed by the group.
   CV and CH will initiate the documentation and the idea is to re-discuss about this documentation offline and then discuss it in the group.
6. **Kickoff Meeting**. LV proposed a Kickoff meeting online with all laboratories of the duration of 1 day - 2 hours to introduce all the different labs and provide some general info of timeframe activities, collect questions from the laboratories, and then present on a second meeting the details of the study design and the SOPs.
   LV will start to organize the kickoff meeting to introduce each other follow by another meeting specific once the SOPs are ready.

Christina von Hunolstein
Chair of the PSPT Steering Group



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