

**DCVMN PSPT Project
Technical Workshop 12
Thursday October 28th 2021**

Attendees: Apichai Supasanatorn (ASP), Arjen Sloots (AS), Arun Bhardwaj (AB), Christina Von Hunolstein (CVH), Deepak Mahajan (DM), Dewi Sulanjari (DS), Elizabeth Ika Prawahju (EP), Erti Resnawati (ER) Gautam Sanyal (GSL), Gopal Singh (GSH), Irma Riyanti (IR), Muhammad Erdiansyah (ME), Pradip Das (PD), Pavel Mitrenga (PM), Pavlinka Stoyanova (PS), Praveen Vittala (PV), Ratih Pujilestari (RP), Sarvesh Tayshete (ST), Sreenivasulu Reddy B (SR), Sunil Gairola (SG), Surender Reddy (SUR), Tim Schofield (TS), Weryarmarst Jaroenkunathum (WJ), Yojana Shinde (YS), Zulfa Noerhidayati (ZN), Laura Viviani (LV), Sonia Pagliusi (SP), Sonia Villaseñor (SV), Sivashen Cunden (SC)
Apologies: Anissa Wari Murti (AWM), Dini Hiayati (DH), Coenraad Hendriksen (CH), Dionne David (DD), Jim Saylor (JS), Maya Ramdas (MR), Rajinder Suri (RS), Ute Rosskopf (UR), Sivakumar Sakthivel (SS), Sekar Thangaraj (ST), Supaporn Phumiamorn (SPH),

Welcome and AOB

CVH

CVH opened session and thanked participants for attendance. No requests for other business were raised.

1. PSPT Project Update

LV

- Currently the project is nearing end of original testing phase, however, this is to be extended to January 2022 to accommodate labs who will require additional time.
- For those labs who have completed testing, their results are to be uploaded to the DCP which is being monitored.

NIIMBL No-cost extension

- No-cost extension of 6 months for the project till July 2022
- The extension was discussed and approved by the SG.

Extension Activities

1. Statistical analysis – Month 17-18
2. Scientific paper submitted and published with open access rights in a Journal (Biologicals or Vaccine)- Month 18-20
3. Technical support for planning full validation studies and additional coating antigen donation - Month 18-20
 - DCVMN will provide support for those labs interested
 - DCVMN will also send additional coating antigen to those labs that will run full validation.
4. Identify opportunities for future Coating Material availability and Management – Month 18-23
5. Project content creation for external communication – Month 18-23
6. Virtual PSPT training content Month 18-23
7. Final Project Workshop Month 22-23
 - WHO, NRA and other relevant parties to be invited to fully present the results and potential of the project and assay

Discussion

- WJ asked if validation study will require participation from all participants.
- LV clarified that the full validation is a voluntary extension project. DCVMN will not be leading the project but will provide the technical support and planning.
- WJ stated that NCL Thailand is interested in the validation but in 2023 not in 2022 due to other project priorities. However, NCL Thailand is interested to attend the planning and support sessions.
- SG asked if the results of the validation study are expected to be shared with the DCVMN.
- LV replied that the results cannot be shared with the DCVMN and should only be shared with your NRA. No statistical support can be given in the validation study.
- LV stated that the WHO will be engaged in 2022 to discuss acceptance of the PSPT into WHO TRS. However, a WHO collaborative study will be required.

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- Those participants who wish to organize a validation study have to provide their response prior to May 2022 as the coating antigen needs to be shipped within the timeline of this project.
- Current MTA will be valid for the shipment to the PSPT members.

2. Laboratories: status of activities

1. CDSCO Kasauli India

- FL3 ELISA to be completed
- Final Results expected in November

2. Biological E Limited

- Results uploaded to the DCVMN DCP.

3. BulBio

- Update to be given offline.

4. Bharat Biotech

- Results have been uploaded to the DCVMN DCP.

5. Biofarma

- Due to variability within the results, Biofarma will evaluate and reprocess data to confirm.

6. Department of Medical Sciences Thailand

- PSPT will be conducted within this week.
- PSPT results to be uploaded in November.

Questions

- NCL Thailand awaiting updated Excel file to allow the copy and pasting of graph.
- LV clarified this will be fixed and new Excel file sent.

7. NCL Indonesia

- Upload of the results will be completed within the next week.
- Lab books are also being reviewed and uploaded.

8. Panacea Biotech

- Results to be uploaded within November.

9. Sanofi

- Experiments are ongoing; currently, the reference standard and positive control sera preparation has been completed and samples will be tested within the week.

10. Serum Institute of India

- Study has been completed.
- Results have been uploaded.
- Combistats results have also been uploaded.

3. Technical Q&A

AS

1. How to address the Outliers (either saturated absorbance at all dilutions or low value in test results, in one of the columns, but not the entire ELISA plate)

- AS asked if this is the case for just one sample dilution or all samples?
- If seen for all samples, AS suggested titrating the conjugates or further dilute the serum

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- If only seen in one sample, this is an outlier and should be considered a hyper responder.
- TS stated that within the Excel file an automatic titer calculation was assigned at 2.5 for non-responders.
- Hyper and hypo responders or any other outliers will be assessed based on the results received during the statistical analysis.
- All participants in agreement with the proposal that outliers will be addressed in statistical analysis by TS.

2. In potency calculation sheet, Reference standard potency is given as IU/vial, can it be IU/ml?

- AS answered yes, this can be done; however he suggests that this maybe better done during the analysis step to avoid various versions of the Excel file and resubmissions
- TS agrees with AS suggestion as this multiplier can be changed much easier after submission.
- CVH asked what dosage the vial in the spreadsheet refers to 10, 5 etc. as usually this is expressed per dose which is normally 0.5 ml.
- SG in agreement with CVH suggests to convert to IU/ml and additionally the international unit per mouse should be captured.
- All participants agree to postpone the modification of the Excel file and address the IU/ml in the analysis step.

3. In the curve fit graph generated in Excel, can the interpolated samples be verified from the background absorbance or noise.

- YS asked if, in case of non-responders, when it is clear that the absorbance of the sample is equal to the background, there is a formula to determine a cut off and the possibility to exclude that sample from the results calculation.
- TS answered that the Excel file has this function, but if there are concerns, this result should be shared so that TS and AS can review it.

4. How to address non-parallelism issue during the final calculation.

- SII asked if in the Excel file there is a change in results color that indicates non-parallelism.
- TS suggests writing a short note on how to interpret the ANOVA table to determine non-parallelism.
- CVH suggests to calculate the results in Combistats as it provides the indication of non-parallelism

5. Wide differences in LCL and UCL limits needs expert opinion

- TS suggests that after evaluation of the data a threshold can be proposed
- CVH stated that normally for biological assays these thresholds are established at 50%-200% of the estimated value.
- TS stated that this would be determined by the variability of the results and may not need to change but the results need to be reviewed first.
- CVH mentioned, when reviewing the preliminary PSPT results calculated by Combistats by one participant, all acceptance criteria were met using FL1 as the reference standard. Crucially, it needs to be determined, against which reference the potency data will be calculated .

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- AS agrees and suggests that this can be addressed and discussed after all results have been collected.

5. Next steps

- ❖ **All participants should indicate by Dec 2 if they agree with the project extension;**
- ❖ All results should be submitted before to address the questions raised in the Technical Q&A;
- ❖ All participants should remember to upload their lab books on the DCVMN DCP;
- ❖ All participants are invited to send any specific or technical questions via email and in cc to CVH.

Meeting closed at 13:08*Notes taken by SC.**C. v. KH***Signed****CONFIDENTIAL**