DCVMN
Developing Countries Vaccine Manufacturers Network

DCVMN 3Rs Working Group Meeting Q4 Minutes – November 30th 2022

Attendees: Pradip Kumar Das (Biological E) *chair*, Deepak Mahajan (Panacea Biotec), Irma Riyanti (BioFarma), Rajanathan Chozhavel (Zysus Cadila), Gurbaksh Singh (Bharat Biotech), Sunil Goel (Serum Institute of India), Hassan Ahmed (Amson), Mahesh Devaraju (Indian Immunologicals), Laura Viviani (DCVMN) Excused: Zebun Nahar (Incepta Vaccine) co-chair; Rajinder Suri (DCVMN), Indrajeet Poredi (Bionet Asia), Vu Tien Dung (Vabiotech), Taehyun Kim (LG-CHEM), Patricia Carneiro (Butantan), S. Sivakumar (Pasteur Institute of India), Li Yi (IMBCAMS), Lingyun Zhou (Shanghai Zerun Biotechnology)

Brief introduction of participants and agenda

Pradip Das (PD) welcomed all participants and introduced the agenda.

1. **Internal Activities Updates**
   - Single Dilution Assay Project
   - PSPT – update on the publications
   - DCVMN 3Rs manuscript
   - MAT feedback from DCVMN members Updates on ATT, PSPT and other opportunities
   - Single Dilution Project
2. **External Activities Updates**
   - NC3Rs Project
   - World Vaccine Congress – session on regulatory alignment on 3Rs
   - HSI/AFSA projects (ATT and a new one – opportunity for DCVMN to participate)
   - BSP148/Rabies
   - DT in vitro potency test
   - MAT and rFC opportunities for dialogue (EDQM/EPAA hybrid conference February 2023)
3. **2023 Focus**
   - Complete SDA Project
4. **AOB**

1. Internal Activities Updates

LV updated the working group on the status of the Single Dilution Project. The open call took place on October 28th, where all the participants (experts from Sciensano, expert from Biological E, Serum Institute of India and Sanofi India, 5 DCVMN companies) of the project introduced themselves. A technical workshop was hosted by DCVMN on November 22nd, where experts from Sciensano presented the technical details of the implementation of the Single Dilution Assay for Tetanus and Diphtheria and shared the spreadsheet that participating companies have to fill by next January 13th, 2023.

LV reported about the status of the PSPT publications: 1) the project results manuscript is almost ready to be submitted, the Steering Group is finalizing the results and discussion part of the manuscript; 2) coating antigen manuscript is on a draft stage and might require additional work before the submission. LV informed about the delay experienced for the transfer of the remaining coating antigen vials from BioLyo (Belgium) to NIBSC (UK) due to some reorganization in NIBSC. If companies are interested to get additional vials before they're transferred to the UK, they can get in touch with BioLyo (Ms Liesbeth Vercruyssen - liesbeth@biolyotech.com). The cost of the shipment must be sustained by the company. LV reminded the companies that the use of the coating antigen is for research purpose only, and not for batch release testing. The produced and characterized coating antigen is not an official standard approved by WHO or local authorities, and there is no agreement with BioLyo to have more batches of coating antigen produced. PD reminded that the best approach would be to calibrate an internally produced coating antigen with the one produced by BioLyo and characterized by Intravacc. LV thanked all the companies that are continuing the PSPT optimization and wish to validate the method.

LV reminded the working group members to review the 3Rs Manuscript and to send her the approval to be listed as author by December 2nd, 2022. She will submit the manuscript to Biologicals (open access).

LV reported on the limited feedback received on the difficulties experiences on the implementation of the Monocyte Activation Test. She thanked for the received feedback and she will inform the interested companies about the possible

solutions after having consulted experts in Europe. She reminded about the materials that has been created after meetings in Brazil, organized by Humane Society International, that could present similar challenges and some recommended solution by experts from BraCVAM (Brazilian Center for Validation of Alternative Methods). LV will share the material once translated. LV clarified that if a product is already release with BET, so the product has no (or limited risk) of NON ENDOTOXIN contaminants, MAT is not needed because MAT replaces the Rabbit Pyrogenicity Test not the Bacterial Endotoxin. In case of new products, MAT can be used during product development to establish whether the product's components are pyrogenic or if the production process might introduce non endotoxin contaminants. In such case, MAT can serve as a tool to define the product's safety (and testing) specifications. If MAT demonstrate limited risk of contamination, the product can be registered and released with no RPT/MAT. She mentioned an important hybrid conference: **EDQM–EPAA event on the future of pyrogenicity testing: phasing out the rabbit pyrogen test, 14 to 16 February 2023** that will present the work ongoing within EDQM to completely replace the Rabbit Pyrogenicity Test by 2026. She mentioned that the Indian Pharmacopoeia has important chapters for comments: the guideline on the substitution of in vivo with in vitro assay for quality control of vaccines and the guideline on the Bacterial Endotoxin. She strongly recommended to participate to the consultation.

2. External Activities Updates

PD shared an update on the status of the activities within the NC3Rs/WHO project. The working groups are discussing about the recommendations on the alternative methods to be included in the WHO TRS. NC3Rs plans to submit the recommendations next year to be approved by ECBS and might get in the public consultation process and hopefully the entire review process won't go beyond 2025.

LV reported on the interesting session led by DCVMN at the World Vaccine Congress in Barcelona, on October 14th, were stakeholders from EDQM, US FDA, IFPMA, WHO and the Bill & Melinda Gates foundation agreed on the need to harmonize regulations to facilitate implementation of non-animal testing batch release testing.

LV reported about the activities ongoing within Humane Society International/AFSA with regards the deletion and waiver of Abnormal Toxicity Test (overall country specific requirements/industry experience is available here). She mentioned that a new project has started to support industry and regulatory stakeholders to create 3Rs implementation plans in some key countries around the world. Presentation of the project will be done in an ad hoc meeting in mid January 2023. LV will share the invitation to the meeting, all interested companies can get in touch with her.

LV mentioned that it is not possible to organize a webinar on the BSP148 on the replacement of the Rabies NIH Test with a glycoprotein ELISA because the statistical analysis is ongoing, and the data will be presented officially only when the analysis is completed, and all the participants agreed to share the results. That might happen around the end of 2023. Many DCVMN members are participating to the project.

Other news reported by LV are:

- EDQM is considering initiating a Biological Standardization Program on the in vitro potency test for DTP vaccines. Further information will be shared by LV once available.
- AFSA/HSI/BraCVAM WG on MAT in Brazil – materials will be translated in English and made available on AFSA website soon
- rFC – Korean Pharmacopoeia will include recombinant Factor C (rFC) in 2023; Indian Pharmacopoeia is gathering information on rFC method and discussion of its inclusion might come ups in the next future
- SAVE THE DATE: Joint EDQM–EPAA event on the future of pyrogenicity testing: phasing out the rabbit pyrogen test – 14-16 February, 2023 // Brussels, Belgium and online - https://www.edqm.eu/en/w/save-the-date-joint-edqm-epaa-event-on-the-future-of-pyrogenicity-testing-phasing-out-the-rabbit-pyrogen-test?p_l_back_url=%2Fen%2Fsearch-edqm%3Fq%3DEPAA
- Globally Harmonized Specifications: Current State and Future Opportunities, January 10-12, 2023 - Basel, Switzerland – Hybrid - https://globally-harmonized-specifications-basel-2023.iabs.org/
- Maintaining the Quality of Vaccines through the Use of References Standards Current Challenges and Future Opportunities, June 21 – June 22, 2023 - Ottawa, Canada, https://reference-standards-ottawa-2023.iabs.org/

3. 2023 Goals

LV informed that the priority will be to complete the Single Dilution Project by Q2 2023, and she proposed to organize again members webinars where companies can report about their successes and challenges in implementing 3Rs in

their batch release testing. She mentioned that DCVMN will ask to have new chair and co-chair and reconfirm the WG members. A dedicated communication will follow before the end of the year. LV thanked all the WG members for their commitment to the 3Rs and their active participation to this working group, she thanks the chair and the co-chair for their support and coordination.

The meeting was adjourned 14:07 CET.

Signature

12.12.22

Pradip Das

Chair 3Rs WG