Developing Countries Vaccine Manufacturers Network

DCVMN 3Rs Working Group Meeting Q1 Minutes – February 23rd 2022

Attendees: Pradip Kumar Das (Biological E) *chair*, Zebun Nahar (Incepta Vaccine), Deepak Mahajan, Thirunavukkarasu Angappan (Panacea Biotec), Irma Riyanti (BioFarma), Sureshbabu Rajan, Rajanathan Chozhavel, Priyanka (Zydus Cadila), Li Yi (IMBCAMS), Gurbaksh Singh (Bharat), Sunil Gairola, Sunil Goel (Serum Institute of India), Adhir Chaubal, Leena Madhuri (Indian Immunologicals), Matheus Trovão de Queiroz (Butantan), Hassan Ahmed (Amson), Lingyun Zhou (Shanghai Zerun Biotechnology), Laura Viviani (DCVMN), Sonia Villaseñor Excused: Sivashen Cunden (DCVMN), Sonia Pagliusi (DCVMN), Rajinder Suri (DCVMN), Indrajeet Poredi (Bionet Asia), Vu Tien Dung (Vabiotech), Taehyun Kim (LG-CHEM), Patricia Carneiro (Butantan), S. Sivakumar (Pasteur Institute of India).

Brief introduction of participants and agenda

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

1. Cost Saving Data Collection
2. Deletion of Abnormal Toxicity Test
3. DCVMN/NIIMBL Pertussis Serological Potency Test (PSPT) Project
4. DCVMN Workshop on DT Single Dilution Assay
5. NC3Rs/WHO Project
6. VAC2VAC project - Vaccine batch to vaccine batch comparison by consistency testing
7. DCVMN 3Rs Workshops
8. AOB

1. Cost Saving Data Collection

Laura Viviani (LV) thanked all the companies (6) that shared their Business-related aspects of 3Rs implementation (savings in USD). LV mentioned two examples (ATT and Rabbit Pyrogenicity Test) where the cost savings differ up to 2/3 digits: saving on ATT per batch from 7 to 64 USD, and savings on Rabbit Pyrogenicity Test per batch around 100 USD. She asked which parameters might be responsible of such differences, for example the cost of animals might vary whether a company has an internal animal breeding facility or procure animals from an external supplier(s).

- Sunil Gairola (SG) commented on the importance to use the number of animals spared as main data to show impact of the implementation of the 3Rs principle. LV commented that that data is fundamental, however it is important to communicate business data as a way to convince new DCVMN members to consider investments on 3Rs opportunities, as well as the regulatory compliance and alignment argument should be the one guiding the dialogue
- Gurbaksh Singh (GS) informed that Bharat has reported the overall cost reduction including the cost of the test, manpower, animal facility related costs, etc.
- ACTION: the 3Rs WG agreed that DCVMN will get in touch with the companies that has submitted cost saving data to clarify their submission and divide the business cases based on internal or external animal procurement, and review cost saving data, based only on animal-related costs.

2. Deletion of Abnormal Toxicity Test

LV informed about the follow up actions agreed during the AFSA/EFPIA workshop **"Accelerating Global Deletion of the Abnormal Toxicity Test. Planning common next steps"** *on October 14th, 2021* (all materials available here: https://www.afsacollaboration.org/biologicals/att-deletion-workshop/). Commitment was taken to engage WHO and participate to the International Conference of Drug Regulatory Authorities (ICDRA) and International Coalition of Medicines Regulatory Authorities (ICMRA) and include ATT and in general 3Rs within their agendas. WHO has been already engaged but a decision about ICDRA date (2022 or postponed to 2023) and venue (online or face to face) has not yet been taken by WHO. DCVMN is invited to participate to an alignment call with AFSA/HSI, EFPIA on March 3rd to discuss about next steps. DCVMN is also invited to collect additional data about performance of ATT (local and export; experience on waivers; etc.) and the WG agreed on the data collection (ACTION for DCVMN to contact all network).

3. DCVMN/NIIMBL Pertussis Serological Potency Test (PSPT) Project

- Laboratories' testing phase completed
- Statistical Analysis by independent consultant ongoing
- 31 March 2022 – Workshop with preliminary data presentation, assay improvement recommendations (in view of validation plans)
- Documentation review; peer-reviewed publication; communication materials to promote project's outcomes
- Final meeting week of July 4th - SAVE the DATE

- Face to Face in New Delhi – if minimum number of participants reached
- Online event (over 2/3 days for 2/3 hours per day)
- Meeting open to external stakeholders and all DCVMN interested members

DCVMN 3Rs WG members invited to participate, if interested, to the final meeting (please inform LV). LV highlighted how the project is key to speed up the implementation of 3Rs because of the assessment of the method performed by both manufacturers and their NCLs which can facilitate the product specific validation and regulatory acceptance.

4. **DCVMN Workshop - Implementation of the single dilution assay for *Diphtheria* and *Tetanus* containing products – January 27th, 2022.**

LV reported about a successful workshop with 48 participants from 12 companies, with 9 DCVMN members interested in participating to a dedicated project. The objective of the dedicated DCVMN project is to support members to plan the implementation of the single dilution assay for the DT-containing vaccines. DCVMN has submitted a request for funding to cover the technical and scientific support of external experts: Italian Institute of Health/Italy and Sciensano/Belgium have been contacted to enquire about their experts' availability. DCVMN welcomes its members that has already successfully implemented the assay to contribute to the technical and scientific support.

WHO has been informed about DCVMN project and welcome the initiative. Via WHO, DCVMN received the presentation from Sciensano used to train WHO/NCLs.

DCVMN is going to update the network whether funding is approved and will start the defining the project plan.

5. **NC3Rs/WHO Project**

Pradip Das (PD) and SG reported about the importance of the project in updating the WHO Technical Report Series and facilitating local regulatory authorities to align. DCVMN, through its members which are part of various working groups, will continue to collaborate with NC3Rs. PD recommended all WG to register and participate to the NC3Rs regional workshops: European workshop on March 2nd and the and Asian region workshop on April 28th 2022 (https://www.nc3rs.org.uk/events/nc3rs-workshop-implementing-3rs-who-guidelines-understanding-impact-quality-control-and).

6. **VAC2VAC project - Vaccine batch to vaccine batch comparison by consistency testing**

PD reported about the final meeting of the VAC2VAC project that took place on February 15th and 16th, 2022. The main achievements reported were for the DTaP vaccines where NIBSC/UK reported about the characterization of antibodies of the D and T component that could lead to the substitution of the current in vivo assay with a full in vitro one (Characterisation of tetanus monoclonal antibodies as a first step towards the development of an in vitro vaccine potency immunoassay (Riches Duit and Hassall, et al 2021); Characterisation of diphtheria monoclonal antibodies as a first step towards the development of an in vitro vaccine potency immunoassay (Riches-Duit and Hassall, et al 2021)). LV reported about the achievements for the TBE vaccines: both the MAT and an in vitro potency assay have been successfully developed. Other important achievements were presented on the veterinary vaccines area where cell-based assays were developed for safety testing of *clostridial* vaccines and for the rabies vaccines, product specific ELISA has been successfully used by manufacturers (and approved by regulatory authorities). LV invited to closely follow VAC2VAC website where all the publications are available and new ones are expected within the 2022 (http://www.vac2vac.eu/publications). Additional events to promote dissemination of the VAC2VAC accomplishments will be organized by IABS and HSI, and DCVMN will be involved.

7. **DCVMN 3Rs Workshops**

PD and LV enquired about the WG interest in organizing dedicated workshops on 3Rs topics. PD suggested that the work done by NIBSC on DT antibodies characterization could be presented more in details to DCVMN, and the proposal has been supported by GS. SG enquired whether WHO TRS mention about the antigen quantification as alternative to potency testing, since DT-vaccines are old product which relies on immunogenicity (antibody response) and not on their quantification. He voiced the concern that if WHO TRS does not include such an opportunity, it might be challenging to have National Regulatory Authorities to accept the method. SG added that the consistency approach should be taken into major consideration, thanks to the amount of available data that companies can provide, in order to support implementation of new methods, such antigen quantification assays. A

clear bridge between antigen quantification and immunogenicity should be made, although it might be very difficult. PD replied that there is not mention about that in the current TRS, however within the NC3Rs project dedicated working group, discussion has been done on the topic, in particular about the consistency approach. It seems that a proposal would be advanced to WHO/ECBS and the immunogenicity assay is going to become "biological test". That will allow to perform various type of tests, including measuring potency as antigenicity assay. PD added that the sentence requiring the correlation of new methods with in vivo assay should be replaced allowing the use of validated in vitro assay. Thirunavukkarasu Angappan (TA) supported PD sharing the case of IPV vaccines where in vivo potency can be correlated with D-antigen assay. ACTION: DCVMN to get in touch with NIBSC and VAC2VAC to organize a dedicated event on DT antibodies characterization.

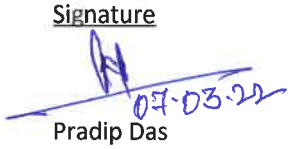
GS asked whether a full in vitro assay might be available for the wP containing vaccines, building from the work done within the PSPT. LV informed the group that she had a preliminary conversation with a group from the New York State Laboratory which is working on DTwP antigen characterization to develop an ELISA (or Luminex) assay. TA expressed interested on in vitro opportunities for DT-containing vaccines. Results of their work is not available, but soon it should be published and there is interest from their side to connect with DCVMN. A dedicated event can be organized as well (ACTION).

PD mentioned that rabies replacement of NIH test is also of high interest. Sunil Kumar Goel (SKG) informed that results of the BSP148 are expected by March/April. DCVMN will follow up with BSP148 leaders and see whether a dedicated event can be organized for the second part of the year.

The next 3Rs WG meeting will take place via Zoom on May 25th, 2022. The calendar invitation has been already sent.

The meeting was adjourned 13:05 CET.

Signature



Pradip Das

Co-chair 3Rs WG