First DCVMN 3Rs Experts Working Group Meeting Minutes  
December 2nd, 2019 - Bangkok

Attendees: Gopahl Singh (Bharat), Kusuma Naidu (Bharat), Sreenivas Kataram (Bharat), GreanggraIHommalai (Bio-Net Asia), Indrajeet Kumar (Bio-Net Asia), Irma Riyanti Hidayat (BioFarma), Nia Kurniati (BioFarma), Pradip Kumar Das (Biological E), Benoit Hayman (DCVMN), Laura Viviani (DCVMN), Somchaiya Surichan (GPO), Wanlop Leeden (GPO), Denis Lambriggs (GSK), Zebun Nahar (Incepta Vaccine), Coenraad Hendriksen (Intravacc), Eliana M. Coccia (ISS), Marilena P. Etna (ISS), Taehyun Kim (LG Chem), Deepak Mahajan (Panacea Biotec), Lavit Jambu (Panacea Biotec), Sivakumar Sakthivel (Pasteur Institute of India), Ratchana Boonmee (QSMI), Sumana Khomvilai (QSMI) – excused, Wachiraporn Hemmala (QSMI), Sunil Goel (Serum Institute of India), Thanh Ngu Nguyen (Vabiotech), Rajanathan Chozhavel (Zydus Cadila).

The proposed objectives of the first 3Rs WG meeting are the following:
1. Learn more about alternative methods opportunities, e.g. DTP and Rabies vaccines;
2. Introduce the Monocyte Activation Test and discuss its use as alternative for pyrogenicity studies;
3. Learn more about the possibility to replace animal use in the manufacturing processes;
4. Establish the Working Group’s priorities and define an action plan for 2020 and beyond;
5. Define the operations and the governance of the Working Group.

Objectives 1-3 have been met through the presentations of the invited speakers, which are available for your consultation at this link: https://www.dcvmn.org/3Rs-Working-Experts-Group-Meeting.

With regards to objective 4, Establishing the WG’s priorities and define an action plan for 2020 and beyond, the WG agreed that the focus of the working group should be on the following tasks:
1. Promotion of 3Rs methods through the interaction with leading expert laboratories worldwide to follow the development and validation of harmonized alternative methods for testing legacy vaccines.
   - It was noted that the relationship between manufacturers and regulatory authorities is challenging because authorities of different countries often have different interpretations on alternative methods, different requirements for their acceptance, and different requirements for filing variation/change request(s).
   - Companies feel more confident in engaging authorities on methods described/listed as compendial in the pharmacopoeia(s) or regulations. Investing in methods not yet compendial places a big burden on manufacturers, as such methods might or might not be accepted.
   - WG would like to gather more information and being more connected with local and international regulators and/or stakeholders in order to build more confidence on the investments on 3Rs. Open point: define what kind of organizations could help in improving dialogue and information exchange.

2. Agreed on initial focus on 3Rs projects specific for DTP-containing vaccines, Rabies and MAT.
   **DTP**
   - Participants confirmed interest on the pilot project on the in-house validation study of the PSPT for wP containing vaccines.
   - Companies also manifested interest in working/investing on a single dilution assay for all the DPT components, but first step will necessarily be an internal assessment of capabilities to take the project onboard in the future (H2-2020).
   - BioNet-Asia is interested in the aP component, but since at the moment in the WG no other companies have aP, there won’t be any activities on that.

   **wP-PSPT in-house validation study**
   - Interested companies: Serum Institute of India Pvt Ltd., Bharat Biotech Pasteur Institute of India, PT Bio Farma*-Indonesia, Panacea Biotec, India, Biological E, India, LGChem*-South Korea.
There is interest for expert consultation to assess current procedures for in vivo testing (submit current in vivo protocol e.g. route of administration).

No need manifested for training on ELISA or in vivo methods.

Need to receive protocols or procedures (SOPs), general guidelines, reagents (coating antigen, capture antibody, pre-estimated standards).

Participants will verify with the companies’ management that testing can be performed within the 6 months’ timeframe – after receiving protocols and reagents.

Regulatory clearance is needed: involvement of NCLs is welcome.

Actions for DCVMN: Secure funds and provide reagents, common protocols and guidelines – Define timelines for the project (Q1-2020).

Action for Companies: get back to DCVMN with management feedback on study participation (in particular for those (*) that still need to get approval) – by 15th Jan 2020.

Rabies

Companies would like to see a harmonized method/protocol and regulatory acceptance for NIH replacement.

Companies producing Rabies vaccines are eager to learn and be informed about the progresses of the ongoing collaborative study (EDQM BSP14) on the replacement of the NIH test with a G-protein ELISA.

At the same time, they wish to learn whether the feasibility study on the PNRT assay mentioned in the last Hyderabad Meeting (June 2019) by WHO has been initiated.

There are presently no specific needs of training, but there is need for SOP/protocols, reagents and materials, once the method is fully accepted by regulators.

Companies discussed on the course of action to take in case a method can’t be used or it is not recognized yet by NRAs. It has been concluded that receiving information is necessary to understand in which testing strategy companies might invest eventually, so regular updates on the topic have been requested (Q2-2020).

MAT

All companies are interested in receiving more information and improve their knowledge in particular in understanding:

- the applicability of MAT to their products (replacing RPT and BET/LAL? When is LAL sufficient? Use of Recombinant Factor C as replacement of LAL?)
- Test specifications, reference standard, cell lines or other reagents availability (any support from DCVMN?)
- It is also important to understand in each region/country whether there could be restriction in using blood products? Availability of blood products? How complicated it is to get ethical approval for use of blood cells?
- ISS is available to provide with information and assess the possibility to propose trainings through webinar or other means to be assessed (Q2-2020).
- The representatives wanted to know, if any manufacturer is already performing BET as a replacement for Pyrogen Test, still replacement of BET with MAT should be justified.

With regards to objective 5. Define the operations and the governance of the Working Group, all members of companies that have not yet nominated an official representative for the WG were requested to proceed with the nomination (31st Jan 2020 – by next WG Call).

The WG will schedule a call every quarter, and at least a face to face meeting once per year. The next face to face meeting could take place in Italy at ISS next spring (TDB with ISS).

Chair and co-chair of the WG are going to be nominated during the next call.

DCVMN wishes to thank Bio-Net Asia for being the host of the WG, all the speakers, all the companies that participated actively to the meeting, and the chair and co-chair of the meeting Dr. Sunil Goel and Dr. Pradip Das, respectively.