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Developing Countries Vaccine Manufacturers Network

DCVMN 3Rs Experts Working Group Meeting Minutes – 2nd Teleconference

July 2nd, 2020

Attendees:
Rajanathan Chozhavel (Zydus Cadila), Pradip Kumar Das (Biological E), Sunil Gairola (Serum Institute of India), Sunil Goel (Serum Institute of India), Taehyun Kim (LG Chem), Deepak Mahajan (Panacea Biotec), Irma Riyanti Hidayat (BioFarma), Dr. Maya Ramdas (Panacea Biotec), Shri T. Sekar (Pasteur Institute of India), Tien Dung Vu (Vabiotech), Srini Kosajaru (Biological E), Nia Kurniati (BioFarma), Adhir Chaubal (Indian Immunologicals), Ganesh Dubey (Bharat Biotec), Sonia Pagliusi (DCVMN), Laura Viviani (DCVMN), Sonia Villasenor (DCVMN- minutes)

Excused:
Indrajeet Kumar (Bio-Net Asia), Anand Kumar Manesh (Indian Immunologicals), Zebun Nahar (Incepta Vaccine), Lavit Jambu (Panacea Biotec), Gopal Singh (Bharat),

Agenda of the second 2020 teleconference 3Rs WG meeting:

1. 3Rs WG next project
2. Brief update on the PSPT project
3. Brief update on the training opportunities
4. DCVMN 3Rs paper - contributions from the WG
5. AOB
6. Important COVID19 information

1. 3Rs WG next project. L. Viviani asked the members of the WG which other projects would they consider important to engage in the future, in order to start to understand and collect our resources for future projects. The intention is to engage the whole DCVM Network because we wish to be sure that our activities are broader and have commitment form more members. We don't have representatives from the rest of the world, only from Asia and from that region we miss China.
   L.Viviani presented some key ongoing projects to help the group to assess the importance of moving towards the 3Rs:
   - WHO/NC3Rs Focus on including 3Rs in the WHO technical report for biologicals and vaccines. The project is to update 60 WHO guidelines. The project will run for 3 years (https://www.nc3rs.org.uk/news/new-project-reduce-animal-use-batch-release-and-quality-control-testing-biologicals). S. Goel is already a member of one of the WHO/NC3Rs working group. DCVMN was also asked to participate, but it is waiting for formal invitation and ToR to see what of experience they are looking for; we might have 3 representatives.
   - From the list of all the opportunities that the group mentioned in our meeting last year, one of the most important was RPT replacement with MAT. In India, it has been replaced with Bacterial Endotoxin test. BET is based on animal reagent. Some synthetic reagents (recombinant Factor C - https://doi.org/10.1371/journal.pbio.2006607) have been developed that are replacing the use of animal based-BET.
   - Indian companies have a strong preference in continuing using the BET, as per the Indian regulatory requirements. MAT is not easy and it has to go through specific product validation; it requires human blood to be used, investment is quite important. L. Viviani said MAT is longer than BET, MAT is to detect any kind of endotoxin and non endotoxin pyrogen contamination, that is why it is so powerful, but it depends on the product production process and risk of contamination. If your products are only endotoxin contamination, you can keep only BET. For viral vaccines BET is enough.
   - Some of the participants (SII, Biofarma) mentioned that If DCVMN has an initiative on MAT, they will follow; the interest is mostly for rabies.
   - L. Viviani asked if there is any interest in rFC. European Pharmacopoeia is enforcing a new chapter dedicated to rFC starting next year. There is a risk of shortage of reagent for BET due to the Covid-19 vaccines productions might increase the demand on the BET reagent and might not be able to cover all the additional request. US pharmacopeia is in more an uncertaln position, planning to have general guidance on how to validate rFC.
   - S. Gairola said SII has almost shifted 99% of products to BET. 1% waiting for regulatory to give the guidelines; any approval goes takes 6 to 7 months so they have taken 2.5 years to shift pyrogen to BET. MAT will be good if 100% 3Rs.

- L. Viviani said that we do not have information on what is happening in China, it seems that they are including MAT in their pharmacopeia but don't know if someone is already performing it.
- Humane Society International is organizing a WG in China with regulators and will be able to learn more about that. BMGF and NC3Rs are going to be part of that WG.
- S. Pagliusi mentioned that we should have a discussion with WHO to ask informally Ivana or Ute if they have any ideas or plans on MAT, regarding pyrogenicity test.
- Regarding DT. L. Viviani mentioned that EDQM is planning in rationalizing test requirements and removing some tests for specific toxicity for Tetanus vaccine and also the test for irreversibility of tetanus toxoid. This summer they will start the review of the requirements for Diphtheria as well.
- Acellular pertussis (aP) will be of interest of some companies in our network and L. Viviani asked if it is in the scope our future plans.
- There is some interest in MAT but before investing in these technologies, we need to understand more. There is interest in rabies. Is there is some things to consider.
- S. Gairola mentioned Implementation of 3Rs in potency testing of rabies vaccine is welcome approach and all manufacturers will benefit. DT is welcome and pertussis; it will be great if Diphtheria review will come soon, as they are the base of hexavalent and if it is done will save a lot of animals.

2. PSPT project. L. Viviani updated the group on the status of the project as mentioned in the slides share to the group. It is important that SII, Biological E, Bharat and Panacea provide their signatures to the Consortium agreement, as we only have 2 and we need at least 5 in order to establish the consortium

3. Training. We have released a new e-learning module in DCVMN Moodle on 3Rs. L. Viviani invited all the participants to get through it and make comments and feedback to correct or add something if necessary. We are preparing another one in aP and there will be a webinar.

4. 3Rs DCVMN paper. L. Viviani and S. Pagliusi mentioned that we started to draft a paper on the commitment of DCVMN on the topic of 3Rs and went through general outline. We will circulate a first draft and then ask for review and comments and fill the gaps. For WG we want to focus on testing activities also there is a lot to do new manufacturing technologies that use animals. We would also want to contribute in this perspective; so we will need a great input from manufacturers.

5. AoB/ Key updates and events about 3Rs. There were no comments.

6. Important Covid19 information. There are 3 opportunities for which the links were shared in the slides. EDQM shared and give free access to their quality standards and you can download some parts of the pharmacopeia. EMA and Korean ministry of FDA to share confidential covid-19 information; and the World congress on alternative methods will have a webinar, if you click the link you will see the details.

- S. Pagliusi mentioned an email from Cristina von Honulstein (ISS, Italy) of Hepatitis A in vitro potency test discontinuation due to the lack of a critical reagent. We will discuss about it in the next meeting.
- S. Gairola mentioned there is being an update about the Indian pharmacopeia. The Abnormal Toxicity Test it has removed from vaccine requirements. Hopefully other regulatory will follow in other countries. WHO has already recommended its deletion.

- R. Chozavel mentioned that NIBSC already provides coating antigen and reference standards for establishing Hep A in vitro test. Zydus is in phase 1, doing correlation studies.

The meeting was adjourned.
Next meeting PSPT kickoff meeting in August just after signature. We can invite observers.
Next 3Rmeeting is at the beginning of October.

Dr. Sunil Gairola
Serum Institute of India
Chair of the 3Rs WG