Second 3Rs WG Meeting
Teleconference

7th May, 2020

Developing Countries Vaccine Manufacturers
Network International
Agenda

1. PSPT Project - NIIMBL has approved it!
   1. 3Rs WG: approval of the Draft Consortium Agreement
   2. 3Rs WG: approval of the proposed Steering Group
   3. Presentation of the next steps

2. Presentation of the MoU with Humane Society International

3. Updates on the training opportunities that will be available within 2020 (MAT, DT, etc.)

4. 3Rs WG suggestions on engaging DCVMN members from other regions

5. AOB/ Key updates and events about 3Rs
1.1 Approval of the Draft Consortium Agreement

• Summary of the feedbacks received so far: minor changes, clarification about the budget, some questions about any IP rights within the consortium

• Next step: distribute the final version+annexes for final review

• Routine for signature’s collection

• Any other clarifications needed?
1.2. Approval of the proposed Steering Group

Role of the Steering Group

*Secure the scientific and technical oversight of the project.*

Meetings: 4 times per year (virtually or in person). Additional meetings may be called by two or more Consortium Parties or on the advice of the Project Manager. The Steering Group may choose to take advice from third parties, if required.
1.2. Approval of the proposed Steering Group

Steering Group

Chairperson: Christina von Hunolstein – ISS, Italy
Co-chair: Arjen Slooth – Intravacc
Members: Sunil Gairola (SII, Chair DCVMN 3Rs WG), Stanley Deming (statistician), member of one NCL participating lab (TBC)

Observers: WHO, NCL not participating lab (TBC)
1.3. PSPT next steps

- Administrative phase (budget and timelines review, contracts signatures (NIIMBL, Eurofins, statistician, etc.)
- Signature of the Consortium Agreement between participating laboratories
- Select dates for the kick-off meeting and preparation
International *in-house* validation of the Pertussis Serological Potency Test (PSPT) in mice to replace the *in vivo* challenge Mouse Protection Test (MPT) in whole-cell Pertussis (wP) vaccine batch testing.

**DCVMN International**

**Proposed Approach:**
In-house validation of PSPT aims to refine the MPT which is highly variable, has poor reproducibility, frequently fail in meeting the statistical validity, uses extensive numbers of animals (150-200 per test) which experience severe pain and distress. MPT raises safety concerns because of the use of virulent *Bordetella pertussis* and has technical complexities (intracerebral injection).

The aim of the study is to demonstrate the validity of the mice-PSPT for discriminating between potent and sub-potent products. Each participating laboratory is performing the tests only with their own products. Since the study will include a regional reference vaccine, it also will enable to relate potency estimates of the MPT with potencies of the PSPT within each participating laboratory. The in-house validation is meant to show the feasibility of PSPT for consistency testing.

Independent statistical analysis is going to be performed.

**Project Plan:**
- **Deliverable 1.0:** DCVMN to establish a consortium with participating laboratories. Month: 1
- **Deliverable 1.1:** Definition of the study design. Months: 2-3
- **Deliverable 1.2:** Production of 2000 vials of wP Coating Antigen (strain 18323) and suitability for use of the material. Months: 2-6
- **Deliverable 1.3:** Coating Antigen shipped to all laboratories of the consortium. Months: 6
- **Deliverable 2.0:** Preparation of the batches and testing. Months: 7-12
- **Deliverable 2.1:** Data collection from the consortium participants. Months: 11-12
- **Deliverable 3.0:** Statistical Analysis. Months: 13-14
- **Deliverable 3.1:** Short report on the study. Months: 14-18

**Project Duration:** [Months 18]  **Project Start & End Dates:** [06/01/20 – 11/30/21]

**Impacts:**
- In-house validation of a new method (PSPT) for developing countries vaccines manufacturers and NCLs
- Manufacturers gain hands-on confidence on the method and gather key validation data to present to regulatory authorities
- NCLs gain confidence on the method and share their experience within WHO-NBB
- Accelerate regulatory acceptance of the PSPT
- Guarantee the reagents’ availability
- Reduce tests variability and repetitions
- Reduce costs and release time
- Refinement of animal procedures

**MRL Level:** [4-7]

**Topic Area:** [Reduce and refine an *in vivo* intracerebral challenge test for batch testing in vaccine manufacturing quality control, used particularly in developing countries ]

**Project Team:**
- Sonia Pagliusi, project and administrative director
- Laura Viviani, senior project management
- Benoit Hayman, project associate
2. Presentation of the MoU with Humane Society International

• cooperation in the promotion and dissemination of information related to 3Rs in vaccine production and testing;
• reinforce dialogue between manufacturers and national and international regulatory agencies/bodies to foster the validation of non-animal based methods;
• promote the implementation and regulatory acceptance of said methods;
• facilitate dialogue between stakeholders at regional and international level, with the aim of fostering a process of alignment of the vaccine's release requirements;
• such other areas as may be agreed between the Parties.
MEMORANDUM OF UNDERSTANDING
BETWEEN
HUMANE SOCIETY INTERNATIONAL
AND
DCVMN INTERNATIONAL
ON
GLOBAL ALIGNMENT OF 3RS OPPORTUNITIES IN VACCINES TESTING

This Memorandum of Understanding (this “MoU”) is entered into between

HUMANE SOCIETY INTERNATIONAL, a not-for-profit corporation established under the laws of the District of Columbia, with its headquarters at 1255 23rd Street NW, Suite 450, Washington DC 20037, UNITED STATES OF AMERICA, (“HSI”) and

DCVMN INTERNATIONAL, a non-profit association of corporate vaccine manufacturers legally established on 15th February 2012, according to articles 60 to 79 of the Swiss Civil Code¹ and existing under the laws of Switzerland, whose address is Route de Crassier 7, CH-1262 Nyon, SWITZERLAND ("DCVMN").
About the Humane Society family of organizations

→ HSI & HSUS together represent the largest force for animal protection globally, active on the ground in >60 countries across the Americas, Europe, Asia & Africa

→ Our science team brings together experts in human & environmental toxicology, regulatory science, public policy, law, biomedicine, etc.

→ Working with lawmakers, regulators, industry, test developers & other stakeholders

→ Stakeholder status with the United Nations, OECD, governmental & corporate advisory bodies on alternative methods & product safety, etc.

ADVANCING HUMAN-PREDICTIVE APPROACHES IN TOXICOLOGY & BIOMEDICAL RESEARCH WORLDWIDE

REGISTERED OFFICES
- Australia
- Belgium
- Canada
- Costa Rica
- Germany
- India
- Italy
- Mexico
- South Africa
- South Korea
- United Kingdom
- United States
- Viet Nam

COUNTRIES WITH RESEARCH & TOXICOLOGY CONSULTANTS OR ACTIVITY
- Brazil
- Chile
- China
- Japan
- Philippines
- Portugal
- Sri Lanka
- Switzerland
Vaccines - Issue overview

- 10-15 million animals used for batch release testing*
- Final animal-based batch release testing is still viewed as the ‘gold standard’ in many countries
- Legacy vaccines: fundamental vaccines for worldwide health safety & highest consumption of animals; also where we can have the most significant economic, safety & availability impacts
- 3Rs + consistency approach being introduced & sometimes implemented in WHO, OIE, EU, US, Canadian & Indian regulations; others are considering it
- 3Rs + consistency approach can significantly reduce the cost of vaccines eliminating, reducing/replacing *in vivo* testing & can reduce lead-time of batch release**

* EPAA. It is an estimation: few countries/regions collect precise numbers of animals used for research purposes
** ~$1K USD for a 28 days batch release test in India vs 5 USD for 1 day in vitro potency test. Source Vaccine Manufacturer, India
Identify ‘RIPE’ 3R opportunities

- Deletion/waiving of Abnormal Toxicity & Target Animal Batch Safety tests
- Replacement of Rabbit Pyrogen & LAL tests with Monocyte Activation Test or recombinant Factor C.

Engage & inform key stakeholders

- Recruit interested regulators, companies & other stakeholders
- Host workshops to share best practices, success stories, identify barriers & possible solutions
- Peer reviewed publications

Effect & communicate policy change

- Advance changes to national regulations, pharmacopoeia monographs/test guidelines, etc.
- Communicate best practices via updated AltTox database (in development)

* Secured >500K USD funds from Bill & Melinda Gates Foundation to advance ATT/TABST work in Brazil, India, Indonesia, China & S. Korea till 2022.
The AFSA Collaboration works to accelerate global adoption of a modern, species-relevant approach to safety assessment that will better protect people and our planet, and hasten the replacement of animal testing.
3. Updates on the training

• 3Rs general e-learning module (DCVMN Moodle) by Prof. Coeraad Hendriksen – Q2
• MAT – webinar/e-learning course and video (pending signature MoU with ISS, Italy) – Q3
• DT alternative methods (pending signature MoU with ISS, Italy) – Q3
• Acellular Pertussis (ongoing discussion with expert) – Q4
• Rabies – Q4/2021
• Vac2Vac Outcomes – Q4/2021 (European Vaccine Initiative)
4. How to engage DCVMN members from other regions

Current members:

• Bangladesh (1)
• India (7)
• Indonesia (1)
• Thailand (1)
• Vietnam (1)
• South Korea (1)
4. How to engage DCVMN members from other regions

Suggestions?
5. AoB/ Key updates and events about 3Rs

IABS Conference, Bangkok, 3-4 December 2019 – report will be published in Biologicals (work ongoing)

http://wc11maastricht.org/ - POSTPONED to 2021
5. AoB/ Key updates and events about 3Rs

Any updates from your countries?
Pharmacopoeias’ update?
Industry/Regulators meetings?
Conferences?
THANK YOU