

VETERINARY
VACCINOLOGY
NETWORK



European Veterinary Vaccinology Workshop

Minutes

21-22 May 2018
The Roslin Institute, UK



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2. Agenda

DAY 1 – 21st May 2018

Room: Auditorium G-022. Animators and chairmen: Bruno Goddeeris (KU Leuven, Belgium) and Gary Entrican (The Moredun Institute, UK)

08:00-08:45	<i>Arrival and Registrations</i>
	<u>Isabelle Schwartz</u> , chair
08:45-10:00	Mucosal vaccines in vet species - <i>Eric Cox</i> (<i>Ghent University, Belgium</i>)
10:00-10:15	<i>Coffee/tea break</i>
10:15-11:30	Vaccination at young age - <i>Linda Saif</i> (<i>The Ohio State University College of Veterinary Medicine, USA</i>)
11:30-11:45	<i>Coffee/tea break</i>
11:45-13:00	Socio-economic aspects of vet vaccine development - <i>Camille Bellet</i> (<i>Institute of Infection and Global Health, University of Liverpool, UK</i>)
13:00-14:00	<i>Lunch/poster session from young scientists</i>
14:00	<i>Group photo</i>
	<u>Jacqui Matthews</u> , chair
14:15-15:30	Anti-parasite vaccines - <i>Damer Blake</i> (<i>Royal Veterinary College, UK</i>)
15:30-15:45	<i>Coffee/tea break</i>
15:45-17:00	Regulatory aspects of veterinary vaccine development - <i>Andy Peters</i> (<i>University of Edinburgh, UK</i>)
17:00-17:15	<i>Coffee/tea break</i>
17:15-18:00	Career opportunities for young scientists. <i>Case studies with Christine Burkard</i> (<i>The Roslin Institute, UK</i>), <i>Carmen Galan</i> (<i>Ingenasa, Spain</i>) and <i>Arnaud Martzolff</i> (<i>Virbac, France</i>).

DAY 2 – 22nd May 2018

Room: Auditorium G-022. Animators and chairmen: Bruno Goddeeris (KU Leuven, Belgium) and Gary Entrican (The Moredun Institute, UK)

8:45-10:00	<u>Madeleine Clark, chair</u> Strategies for inducing broad immunity - <i>Davide Corti (HUMABS, Switzerland)</i>
10:00-10:15	<i>Coffee/tea break</i>
10:15-11:30	Vet vaccines in the One health perspective - <i>Angie Colston (Global Alliance for Livestock Veterinary Medicines, UK)</i>
11:30-11:45	<i>Coffee/tea break</i>
	<u>Bryan Charleston, chair</u>
11:45-13:00	The ToolBox for investigating vaccine responses in livestock species - <i>Jayne Hope (The Roslin Institute, UK) and Anna Raper (The Roslin Institute, UK), John Hammond (The Pirbright Institute, UK) and William Mwangi (The Pirbright Institute), Norbert Stockhofe (Wageningen University, The Netherlands)</i>
13:00-13:10	Presentation of the International Veterinary Vaccinology Network - <i>Carly Hamilton (The Roslin Institute, UK)</i>
13:10-14:15	<i>Lunch/poster session from young scientists</i>
14:15-15:30	Modeling in vet vaccine response - <i>Andrea Wilson (The Roslin Institute, UK)</i>
15:30	Wrap-up

3. Minutes

The Workshop was organised in order to provide integrated and up-to-date knowledge on the challenges facing the development of effective veterinary vaccines.

This workshop was targeting early career and senior scientists and other members of the animal health profession from public and private organisations.

This event was organised by:

- The H2020 SAPHIR project
- The UK Veterinary Vaccinology Network
- The H2020 PARAGONE project

The workshop was chaired by Isabelle Schwartz for H2020 SAPHIR project, Jacqui Matthews for H2020 PARAGONE project, and Bryan Charleston and Madeleine Clark for the UK Veterinary Vaccinology Network.

The presentations are available on SAPHIR, PARAGONE and the UK Veterinary Vaccinology Network websites.

3.1. Mucosal vaccines in vet species – Eric Cox

The first presentation was made by Eric Cox from Ghent University (Belgium). His presentation focused on mucosal vaccines in veterinary species. The main points to keep in mind are:

- While animal vaccination is being developed, birds are the best studied animals for mucosal vaccination
- The challenges of mucosal vaccination are to identify protective antigens, efficient delivery systems and adjuvants, and escape maternal immunity
- In sheep, immune responses in lymph following intranasal injection is high (after secondary immunisation). The required volume of intranasal injection in mice is 50µl, representing 200ml in a human. The mucosal adjuvant CTA1-DD works very well in mice. This is not applicable to the pigs
- In the case of oral vaccination, live vaccines are able to cause lesions and activate the immune system but are often not sufficiently virulent. Dead vaccines are not satisfactory due to successive barriers and tolerance mechanisms in the gut
- F4 fimbriae are an efficient tool to study the immune response following oral immunization: they interact with Aminopeptidase N and induce IL17A in naïve PBMCs, which induce a fortification of the intestinal barrier. Other strategies are currently followed.
- Mucosal vaccination can target differentiated tissues

In conclusion, Eric Cox presented the Third Edition of ECMIS about *E.coli* and the Mucosal Immune System which will take place on the 2nd to 5th June 2019.

For more details, please refer to the presentation

3.2. Vaccination at young age – Linda Saif

The second presentation was made by Linda Saif from the Ohio State University College of Veterinary Medicine in USA. Her presentation focused on the maternal vaccines and passive immunity to enteric viral infections. The major points of her presentation are the followings:

- New born are the most susceptible to CoV/RV infections. The mortality is variable according to the presence and levels of passive immunity (among other criteria)
- CoV and rotavirus induce severe villous atrophy and cause disease at a mucosal surface
- Some issues are associated with mucosal vaccination:
 - Active immunity (through oral vaccination) is not effective in field due to high BCoV/BRV antibody seroprevalence in adults
 - Passive immunity through parenteral live vaccines may require higher doses (heifers)
- Maternal vaccination boosts passive lactogenic immunity in seropositive cows
- Several experiments have been performed to design BCoV/BRV vaccines able to protect the calf from birth to at least 3 weeks of age but some questions remain unsolved regarding the development of PEDV vaccines and improvement of TGEV vaccines

- Gnotobiotic piglets served as model to study correlates of Active Immunity to Rotavirus (RV): protective immunity against disease depends on magnitude, location, viral protein-specificity and isotope of the antibody response induced by vaccination
- Supplementation with probiotics improve the host immune responses to RV vaccines (EcN (G-) +/- LGG (G+))

This presentation is not available on public access

3.3. Socio-economic aspects of vet vaccine development – Camille Bellet

The third presentation was made by Camille Bellet from The University of Liverpool. She presented her work on the socio-economic aspects of veterinary vaccine development, performed in collaboration with Jonathan Rushton (LVU). The main aspects of her presentation were:

- A recall of vaccine history with the example of the Smallpox, an infectious disease which historically occurred in outbreaks in Europe in the 18th century
- Veterinary vaccines have served as complement for human vaccines. In particular, Salmonella strains allowed the development of attenuated and activated vaccines
- In 2011, the eradication of the rinderpest supported the western vaccine industry and the creation of the OIE
- The vaccine industry has profoundly changed: efficacy, safety and convenience of vaccines have improved but vaccination technology is still vulnerable (crisis in 2007 at Pirbright)
- The social context (inequalities between countries, gender, army vs low classes, rural vs urban) has a crucial role in the development of vaccines
- The use of social research can help us to explore what is unsaid in the development of vaccines
- The impact assessment's concept is hard to catch: only 22 papers really focus on assessment of economic impact
- Epidemiological studies would help anticipate some crises and instruct guide policy
- Industries are the drivers for the development of vaccines but it would be interesting to understand where the vaccines would allow to make the more substantial profit.

For more details, please refer to the presentation

3.4. Anti-parasite vaccines – Damer Blake

The fourth presentation was made by Damer Blake from the Royal Veterinary College (UK). The main points to keep in mind are the following ones:

- Parasites are still an important cause of morbidity and mortality
- Current vaccines are:
 - Whole live parasite vaccines (*Eimeria* spp.)
 - Subunit proteins (Leishmune, CaniLeish, Barbervax)
 - Subunit recombinant proteins (TickGARD Plus, Cysvax)
- Legislation:
 - 2008: Anticoccidial substances are allowed as feed additives
 - 2016: Revision of guidelines for anticoccidials
- Ongoing work: Transgenic live *Eimeria* vaccines are being developed
- Et-[EmAMA1] parasites induce significant levels of cross protection against *E. maxima* challenge → *Eimeria* can function as vaccine vector
- The uniformity of the response to this vaccine remains to be assessed

For more details, please refer to the presentation

3.5. Regulatory aspects of veterinary vaccine development – Andy Peters

The fifth presentation was made by Andy Peters from the University of Edinburgh. His presentation focused on the regulatory aspects of veterinary vaccine development. The main point to keep in mind are:

- Quality, safety and efficacy are data requirements for the registration of veterinary vaccines in EU

- The rules governing medicinal products in the European Union are gathered in the Volume 6B – Notice to applicants – Veterinary medicinal products. It contains EU routes to veterinary vaccines' registration
- GMP are required in the EU system of veterinary vaccine regulation and manufacture
- The Directives 90/219 and 2001/18 of the EU legislation are relevant to the use of GMOs in veterinary medicinal products
- DNA vaccines: new innovative veterinary products for regulators and not classified as GMOs
- New product development implies some critical decisions

For more details, please refer to the presentation

3.6. Career opportunities for young scientists. Case studies

Christine Burkard (the Roslin Institute, UK), Carmen Galan from (INGENASA, Spain), and Arnaud Martzolff (VIRBAC, France), gave a short presentation of their career specifically addressed to the young scientists.

Christine Burkard: She studied at the Swiss Federal Institute of Technology where she worked on the development of new recombinant virus tools. She realized a MSc in biological chemistry followed by a PhD on corona virus in Utrecht University. Then, she was offered a position in EU ITN Network and realized a Post doc on pig viruses at the university of Edinburgh.

Carmen Galán: She realized a PhD in coronavirus replication mechanism at the Department of Molecular and Cell Biology Spanish National Centre for Biotechnology (Spain). Then, she left Spain for a Post doc at Max Planck Institute of Immunobiology & Epigenetics in Germany. Finally, she integrated a Business School to strengthen her management skills. She is now employed at INGENASA (Spain), where she is working on the development of diagnostic tests for aquaculture.

Arnaud Martzolff: After a master's degree in plant biology at the Louis Pasteur University in Strasbourg, Arnaud worked as research assistant in the Department of Plant Cellular and Molecular Biology (PCMB) of the Ohio State University (Columbus, USA). Then, he realized a PhD in Nantes University (France) on the systemic analysis of carbon and energy metabolism of *Chlamydomonas reinhardtii*. Then, he first worked in a start-up specialized in lipopeptides produced from *Bacillus sp.* in Lille (LIPOFABRIK) and in a biggest company (SANOFI) before joining VIRBAC as Bioprocess development manager in 2016. He is currently in charge of the development of vaccines in a R&D environment.

For more details, please refer to the presentations

3.7. Strategies for inducing broad immunity – Davide Corti

The first presentation of the second day of the workshop was made by Davide Corti from the Swiss Company HUMABS. His presentation focused on the strategies for inducing broad immunity. The main points of his presentation are the followings:

- 52 monoclonal antibodies (mAb) are currently approved
- It is possible to prolong half-life of mAb by point mutations in the Fc (interaction FcRn), glyco-engineering to modify FcR interaction, mutation to avoid interaction with FcR
- Antibody-guided vaccine design:
 - CMV vaccine: development of a pentameric complex of the virus that induces Ab which are 1000 times more efficient to neutralise the virus on fibroblast/epithelial cells than the natural infection
 - RSV: the majority of mAb are directed to the preF. Induction of high NAb responses with stabilised preF
 - BRSV: preF-DS2 construct is the best inducer of NAb in mice and cattle (doi: 10.1038/s41541-017-0005-9)
 - influenza: the stem of HA induces cross neutralising Ab, efficient in ADCC (shown through mutation in ALA motif that prevents IgG interactions with FcR). However, a HA2 vaccine in pigs enhances viral-induced fusion in vitro and disease in vivo = DOI: 10.1126/scitranslmed.3006366. However, the FL6

human mAb anti-HA2 has no detrimental effects in pigs. A trimeric stem (headless) vaccine provides protection with low levels of NAb (phase 3 in humans).

This presentation is not available on public access

3.8. Vet vaccines in the One health perspective – Angie Colston

The second presentation was made by Angie Colston from the Global Alliance for Livestock Veterinary Medicines (GALVmed) in UK. Her presentation focused on the veterinary vaccines in the One Health Perspective. As introduction, she presented the work performed at GALVmed. The main points to keep in mind are:

- GALVmed works through partnerships on the development of vaccines and diagnostics.
- GALVmed uses donor funding to undertake two major avenues of development work: product and market development
- Six diseases have been identified as potentially eradicable: for taeniasis/cysticercosis disease, a strategy for control and elimination of *T.solium* has been available since 2015. Interventions are scaling up in selected countries. This disease is ranked fourth highest out of 31 foodborne hazards
- Separate controlled vaccine studies in pigs were made by four independent research groups in four countries, achieving very high protection. High levels of protection were also achieved using TSOL18. Large field trials were conducted in Peru
- The PC programme support the TSOL18 vaccine (CysvaxTM) and oxfendazole (ParanthicTM) and lead pilot trials including socio-economic impacts of *T.solium* infection
- Challenges to One Health approach are: partnership, commitment, financing, availability of vaccine drug and sustainability

For more details, please refer to the presentation

3.9. The Toolbox for investigating vaccines responses in livestock species

John Hammond and William Mwangi from the Pirbright Institute, introduced the topic on the Toolbox for investigating vaccines responses in livestock species. Roslin and Pirbright are working in a joint effort to coordinate and develop immune reagents. The priorities of this immunological toolbox are the followings:

- Secure current antibodies through sequencing (Pirbright activities)
- Create and maintain a website of available reagents and associated data
- Generate new antibodies (Roslin activities)
- Facilitate screening of uncharacterized hybridomas

Jayne Hope gave an overview of the current and future work that will be performed at the Roslin Institute on the immunological toolbox: priorities will be guided by requirements of the veterinary immunology community but will certainly include pathogen specific reagents (FMDV antigens for example).

Anna Raper reminded the aim of the toolbox: expanding the veterinary reagent portfolio through the production and characterization of desirable reagents. She gave some examples of services offered by the Roslin Institute:

- Monoclonal antibody production: e.g. bovine CD107a
- Assay development: e.g. generation of chicken IL-10 ELISA
- Conjugation service: e.g. novel application of recombinant protein

Finally, Norbert Stockhöfe presented the first results of the Transnational Access Management within Vetbionet-H2020. The overall objective of the European infrastructure project VetBioNet is to establish a comprehensive network of pre-eminent high-containment research facilities, academic institutes, international organizations and industry partners that is dedicated to advance research on epizootic and zoonotic diseases and to promote technological developments.

For more details, please refer to the presentation

[3.10. Presentation of the International Veterinary Vaccinology Network – Carly Hamilton](#)

The International Veterinary Vaccinology Network (IVVN) was presented by Carly Hamilton from the Roslin Institute.

The main characteristics of this network are the followings:

- It was initiated by Dr. Tim Connelley and Dr. Bryan Charleston in August 2017 after receiving £2.2 million from the MRC/BBRSC/GCRF
- The aim of the IVVN is to facilitate the formation of international collaborations to improve vaccine design and development for livestock and zoonotic diseases in low-and-middle income countries
- Until now, IVVN has welcomed 375 members from across 43 countries and new memberships are expected
- Members are welcome to host workshops on specific topics of their choice (open call)
- The next IVVN Conference will be held on the 9th and 10th January 2019 in London
- The second call for IVVN Pump-Priming Grant Applications is open until the 2nd July 2018

For more details, please refer to the presentation

[3.11. Modelling in vet vaccine response – Andrea Wilson](#)

The last presentation was made by Andrea Wilson from the Roslin Institute. Her presentation focused on modelling the vaccine effectiveness in the field. She introduced her talk with a description of the basic principles of mathematical modelling. The key points of her presentation are the followings:

- A mathematical model aims at investigating the properties of a system and always requires simplification
- They are extremely useful in the context of infectious disease characterized by strong experimental constraints
- Epidemiological models enable to determine the risk associated with the occurrence of outbreaks and the impact of vaccination on epidemics. Therefore, they can influence policy decisions but can cause friction
- Several interacting factors affecting vaccine effectiveness in the field (e.g. vaccine properties and administration, environmental effects, herd management, host/pathogen characteristics) can be taken into account in mathematical modelling
- A mathematical model has been developed to assess the effectiveness of attenuated PRRSV vaccine in the field (H2020 SAPHIR Project)

For more details, please refer to the presentation

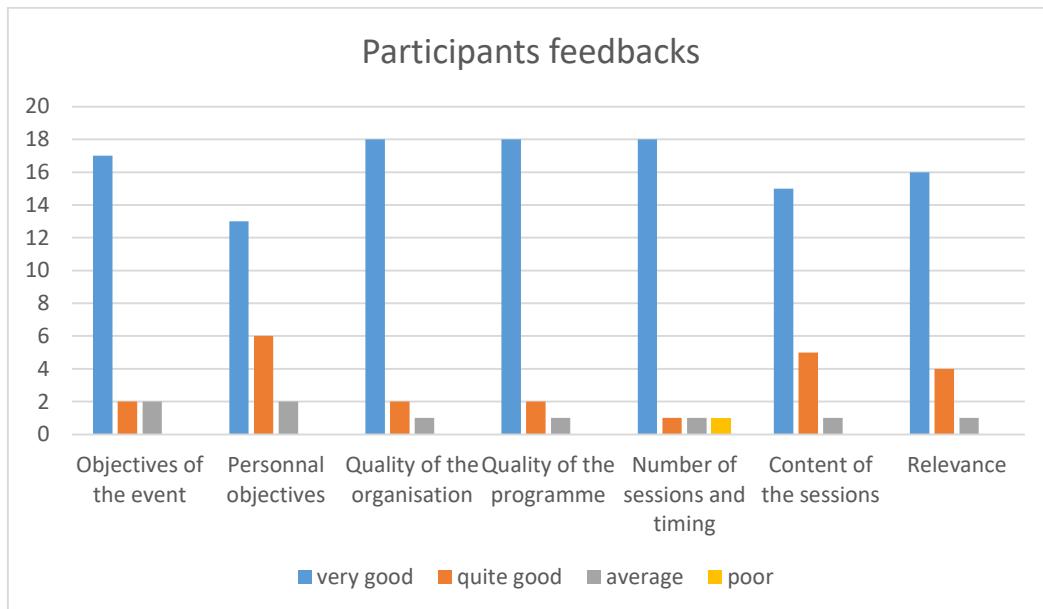
[3.12. Conclusion of the workshop](#)

This workshop allowed fruitful discussions between the attendees and the invited experts. The main conclusions are the followings:

- Developing a vaccine is a complex process and lots of gaps remain in the understanding of the mechanisms involved in the vaccine response
- Involvement of both researchers and industries are needed to achieve successful veterinary vaccine development
- Some vaccines already exist on the market but there is a crucial need to identify new protective antigens, efficient delivery systems and adjuvants: new ideas are being developed
- Finding financial instrument for vaccine development is a critical issue: cost assessment of endemic animal diseases is a key to rise proportionate financial supports

4. Evaluation Feedbacks

Participants of the workshop were invited to fill in an evaluation form in order to provide feedbacks to the speakers and organisers. Main results and feedbacks are presented in the graph below.



The participants were globally very satisfied by the organisation and the content of the workshop. Some feedbacks received on what attendees appreciated the most:

- “Discussions after each talk, frequent breaks between talks, expertise from speakers”
- “Diversity and quality of speakers, length of speech, time to interact during coffee breaks”
- “The global vision of the vaccinology (strategies, socio-economics aspects...)”
- “The case study presentations, it is a good idea to inspire young scientist careers”
- “The time dedicated to questions and exchange”

To improve the quality of future events, the following suggestions were made:

- “Proposing a specific session for the PhD and allowing students to present poster talks in general session”
- “Potentially inviting some scientists from other fields interested in technology development and managing studies as a way to enrich discussions”
- “Including talks about logistics, vaccine distribution chains and vaccine market”
- “Involving vaccine development specialists to present the challenges of the development of an effective vaccine”