SPIDVAC

Newsletter No 4 June 2024

Dear reader,

We are halfway through the project and there is still a lot to do! As is always the case with such large projects, some of the goals we have set ourselves as a consortium are already within reach, while others are still some way off. We need to keep working hard, adapting strategies and implementing new ideas. In addition, of course, we must not lose sight of new developments in the field, such as the emergence of serotype 3 of bluetongue virus in the Netherlands in September 2023 and its continued spread. Some new faces from the project will introduce themselves and we conclude the newsletter with information on conferences and meetings that SPIDVAC members have attended to present their work on AHS, PPR and FMD.

We hope you enjoy reading and look forward to your feedback!

News about notifiable animal diseases / Looking beyond the horizon

Orbiviruses in Europe

Dr. Bernd Hoffmann and Dr. Jörn Gethmann

FLI, Institute of Epidemiology and Institute of Diagnostic Virology

In our last newsletter, we reported on the impressive comeback of bluetongue (BT), a notifiable animal disease transmitted by midges. As was to be expected, the number of animals infected with BT in Germany and throughout Europe has increased as temperatures have risen and the midges have awoken from their winter break.

The bluetongue virus (BTV) diagnosed in the Netherlands at the beginning of September 2023 is of serotype 3, which has so far only been found in Europe in southern Italy. It is a new BTV-3 strain that is not closely related to the Italian BTV-3 strain. Genetically, its closest relatives are BTV-3 strains from Southern Africa, but its route of introduction into the Netherlands remains unclear.

Figure 1 Clinical signs in sheep (salivation, erosion of the oral mucosa and bleeding in the mouth area) and cattle (crust formation on the nostrils and necrosis on the teats). (© "Emergence of bluetongue virus serotype 3 in the Netherlands 1 in September 2023" kindly provided by Dr. Melle Holwerda, Wageningen Bioveterinary Research (WBVR). https://doi.org/10.1101/2023.09.29.560138)

In addition to sheep and cattle, goats, New World camelids and mouflons have also tested positive for BTV-3, although the focus of the clinical manifestation and the number of confirmed infections is clearly in sheep and cattle. Mortality of 20—25% is reported in sheep. Mortality in cattle is currently 1—5%. It is striking in this context that older sheep (> 1 year) and older cattle (> 2 years) are particularly affected with increased mortality.

In addition to the Netherlands, Germany and Belgium, even the United Kingdom was not spared from the introduction of BTV-3. A massive increase in the number of cases is expected in 2024. Infection with BTV is notifiable in Germany. The status "free from bluetongue" has now been revoked in Germany for the states of Lower Saxony, Bremen and North Rhine-Westphalia.

But it is not only BTV-3 that is circulating in Europe. Other orbiviruses are on the rise. BTV serotypes 1, 3, 4 and 8 are widespread in Spain, Italy and France. There was another BTV-3 outbreak in Sardinia, but it is genetically different to the BTV-3 from the Netherlands and apparently causes milder clinical signs. In August 2023, a "new" BTV-8 strain was discovered in southern France, which causes significantly more clinical disease in sheep and cattle (source: Platforme ESA)

In the fall of 2022, infections with epizootic hemorrhagic disease virus (EHDV) serotype 8 were reported for the first time in Italy and Spain. In the fall of 2023, the affected area expanded significantly to the entire Iberian Peninsula and southern France. At the end of 2023, large parts of south-western France were confirmed as EHDV infection areas.

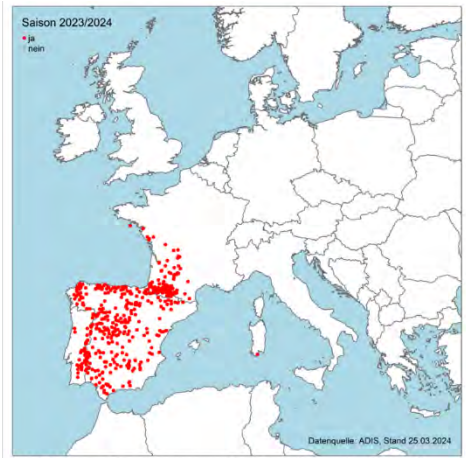

Figure 2 EHDV cases from January 2023 to the end of March 2024 in Europe (© ADIS) kindly provided by FLI/IfE

EHD is closely related to BTV and widespread worldwide, although Europe has so far been spared from the disease. While cattle usually contract the disease sub clinically, infections with EHDV cause severe clinical disease in North American white-tailed deer. However, depending on the EHDV serotype and strain, clinical disease with typical BTV signs can also be observed in cattle. Sheep and goats play no epidemiological role. (More information about EHD in France: Zientara S, et al., 2024, Emergence of Epizootic Hemorrhagic Disease in France in 2023: Impacts and Future Prospects. Virology 28(1):1-2. doi: 10.1684/vir.2024.1035).

Currently, vaccination with inactivated serotype-specific vaccines remains the method of choice for targeted orbivirus control and prophylaxis.

In mid-May, Boehringer Ingelheim released their BULTAVO 3 vaccine against BTV-3 in sheep and cattle. The inactivated vaccine prevents mortality and clinical symptoms in sheep after a single subcutaneous application and in cattle after two intramuscular injections. In addition, the risk of transmission of the BTV-3 virus is significantly reduced as the circulation of the virus in the blood of infected animals is drastically reduced.

The vaccine has been approved for emergency use in the Netherlands and will be available from the end of May 2024. (https://www.boehringer-ingelheim.com/animal-health/livestock/ruminants/vaccine-bluetongue-virus-serotype-3-sheep-cattle)

Author: S. Weber

5 Facts about PPRV

1. Peste des petits ruminants (PPR) is also known as ‘goat plague’, ‘Kata’, ‘syndrome of stomatitis-pneumoenteritis’ or ‘ovine rinderpest’
2. PPR was first reported in Côte d'Ivoire in 1942 and affects goats, sheep, and some wild relatives of domesticated small ruminants, as well as camels
3. Peste des petits ruminants virus belongs to genus *Morbillivirus*, alongside other important viral pathogens, e.g., Rinderpest virus, Measles virus, Canine distemper virus and the Phocine distemper virus
4. WOAH and FAO developed the Global Control and Eradication Strategy of PPR and have set the goal of eradicating the disease by 2030
5. PPR has severe negative socio-economic impacts on the income of livestock farmers and, in particular, the livelihoods and food security of the most vulnerable rural communities, notably of women

Author: S. Weber

On the way to eradicate PPR by 2030

Since peste des petits ruminants (PPR) was first described in Côte d'Ivoire in 1942, the virus has been found all over the world and is currently endemic in over 70 countries in Asia, Africa and the Middle East (WOAH, 2023). The virus, which belongs to the genus *Morbillivirus*, is closely related to the rinderpest virus and is a notifiable animal disease of small ruminants such as sheep and goats. The contagious, transboundary disease has serious negative socio-economic consequences. Small ruminants are of great importance for the livelihood of the population in many regions of the world. They are mainly kept by family farms to produce food and other products such as wool and hides, thus securing their income.

For this reason, the Food and Agriculture Organization of the United Nations (FAO) and the World Organization for Animal Health (WOAH) have set themselves the goal of eradicating this disease by 2030, following the example of the eradication of rinderpest virus. In 2015, high-level representatives from 70 countries approved the Global Strategy for the Control and Eradication of PPR (PPR GCES).

The strategy is based on three interlinked components

- a four-stage technical approach to combating and eradicating the disease
- the strengthening of the veterinary services in order to be able to implement the technical component
- the control of other priority diseases of small ruminants together with PPR to increase the impact of the control measures

The four stages correspond to a combination of decreasing epidemiological risk and increasing prevention and control measures. The phased approach is intended to lead to a gradual reduction in the incidence and spread of PPR through targeted vaccination in the affected countries.

In stage 1, the countries assess their epidemiological situation. In stages 2 (control of PPR infection) and 3 (final eradication through increased surveillance and preventive measures), the focus is primarily on vaccination campaigns. The global rinderpest eradication programme has shown that a highly effective rinderpest vaccine, which can immunize animals against all strains of rinderpest virus, is crucial to the success of the campaign. Effective vaccines are also available against PPRV, which can induce lifelong protective immunity in vaccinated animals. Vaccination therefore plays a central role in the fight against PPR.

In stage 4, a country can then prove that there is no longer any PPR virus circulating and it is therefore ready to apply for the official WOAH status of PPR-free. This multi-stage strategy offers countries the opportunity to skip individual stages. For example, a country that determines in stage 1 that there is no PPR virus circulating can go directly to stage 4.

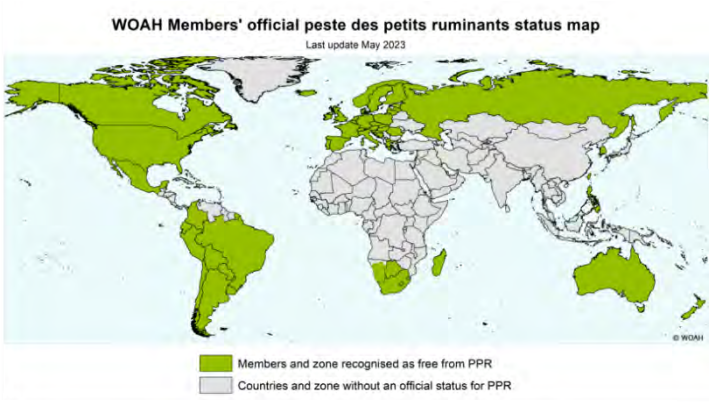

Figure 3 Map of PPR official status worldwide from May 2023 (© WOAH)

In 2015, 48 member countries that have always been PPR-free, including European countries, were on the OIE list of PPR-free countries. According to the WOAH list, a total of 59 countries will be considered PPR-free in 2023.

Author: S. Weber

3 Questions to...

Jean-Francois Valarcher (Scientific Advisory Board)

- What opportunities do you see in the SPIDVAC project?
  A project to develop innovative DIVA vaccines for three major transboundary diseases that significantly impact animal welfare and the economy.
- What is your favorite part of being a scientist in general?
  I am passionate to get a better understanding and control of viral diseases in livestock. My primary interest lies in studying host-pathogen interactions to develop effective vaccines, treatments, and biosecurity measures.
- How would you describe your role as a member of the external Scientific Advisory Board?
  To provide an external perspective on a project and offer the best suggestions to achieve its goals, drawing on my previous experiences.

Who is Who?

Elodie Chapot

My name is Elodie Chapot, I'm based in Lyon (France) and I have worked for Boehringer-Ingelheim Animal Health for 3 years. I started when I was a trainee, working on developing molecular biology tools for vaccine purity testing. After obtaining my master's degree in molecular and cellular biology with a specialization in infectiology, I had the opportunity to participate in different clinical studies. During my last experience, I participated in a molecular biology project and vaccine stability monitoring. I joined the Viral Disease Research (VDR) and SPIDVAC project since the beginning of the year and I'm very happy to contribute and learn more about this project.

Stephanie Blanchard

My name is Stephanie Blanchard, I am a lab expert technician in the VDR team at Boehringer-Ingelheim Animal Health, where I currently focus on baculovirus-based protein expression.

I hold a Master II's degree in animal physiology and toxicology with over twenty-five years of experience in molecular biology, virology and biochemistry acquired in several public research laboratories (CNRS-INSERM) and Merial/Boehringer-Ingelheim Animal Health.

I joined Merial in 2000 as a technician in a molecular biology research lab. After 2 internal missions in immunology and virology research laboratories, I transitioned to a technical scientist position in biodevelopment. In this role, I developed molecular tests for clinical follow-up, purity control, marketing support and research. After providing support in the establishment of the nanoparticle technology in the VDR team, I am excited to join SPIDVAC and bring this technology to the next level.

Working internationally - Introducing the project partners

Boehringer Ingelheim Animal Health

The lives of animals and humans are interconnected in deep and complex ways. We know that when animals are healthy, humans are healthier too. Across the globe, our 9,700 employees are dedicated to delivering value through innovation, thus enhancing the well-being of both.

Respect for animals, humans and the environment is at the heart of what we do. We develop solutions and provide services to protect animals from disease and pain. We support our customers in taking care of the health of their animals and protect our communities against life- and society-threatening diseases.

Boehringer Ingelheim Animal Health is the second largest animal health business in the world, with net sales of 4.1 billion euros in 2020 and presence in more than 150 countries. For more information visit: www.boehringer-ingelheim.com/animal-health/overview.

Author: J. Kortekaas

Outside the lab - SPIDVAC goes to meetings

Greifswald. In December 2023, Michael Eschbaumer (FLI, Coordinator) presented SPIDVAC at the meeting of the Scientific Advisory Board (SAB) of the Friedrich-Loeffler-Institut (FLI). The SAB advises the management of the FLI on research and development planning and annually reviews the research, advisory and service activities of the individual scientific organizational units at the FLI. At the same time, the SAB promotes links between the Federal Research Institute and scientists and research institutions in the same and related scientific fields in Germany and abroad. The majority of the members of the SAB are internationally renowned scientists from Germany and abroad. Stéphan Zientara, a member and co-coordinator of SPIDVAC, is also represented on this important link between the FLI and the scientific community.

In a nutshell

ASFaVIP - African Swine Fever attenuated live Vaccines In Pigs

Since the beginning of 2024, the Friedrich-Loeffler-Institut and colleagues from the Stichting Wageningen Research of the SPIDVAC consortium have been involved in another EU-funded, international cooperation project to develop an orally administered vaccine. In addition to developing a live attenuated vaccine for the prevention and control of African swine fever (ASF) in wild boar and domestic pigs, "ASFaVIP" (African Swine Fever attenuated live Vaccines In Pigs) aims to deepen the understanding of the immune response and to investigate the influence of genetic factors of ASF viruses and hosts in more detail. ASF is a severe and globally significant viral disease of domestic and Eurasian wild boar for which neither therapeutic nor vaccine preventive measures are yet available. While traditional prevention and control strategies work well in industrial pig farms, they quickly reach their limits in wild animals. In Europe, this mainly affects wild boars, but also other endangered pig species worldwide. The development of an orally administered vaccine could therefore also contribute to the conservation of biodiversity. We wish you every success with this project.

More information: https://asfavip.fli.de/de/startseite

Author: S. Weber

Journal Article - Comparative evolutionary analyses of peste des petits ruminants virus genetic lineages

Peste des petits ruminants (PPR) is a highly infectious disease, especially in goats and sheep, that has a significant impact on the economy and food security in large parts of Africa, Asia and the Middle East. To improve the understanding of PPR epidemiology and support ongoing global efforts to eradicate the disease, SPIDVAC partners from Senegal and CIRAD generated the genome sequences for twenty-five current (2010-6) and seven historical (1972-99) PPRV samples to compare the evolutionary pressure between the globally dominant PPRV gene LIV and LII. It was shown that the relationship between the PPRV LII strains is complex and supports the extensive transboundary circulation of the virus within West Africa, whereas the LIV sequences were clearly separated by region. Phylogenetic relationships between historical samples of LI, LII and LIII and more recent samples suggest high genetic diversity for all these lineages in Africa until the 1970s and 1980s.

More information on this exciting field of research can be found in the publication.

https://doi.org/10.1093/ve/veae012

Author: S. Weber