

Dear reader,

Another year is coming to an end and the SPIDVAC project can look back on 18 interesting months. We were all finally able to meet in person at ANSES in Maisons-Alfort, France and got to know each other better on a personal level as well as in a scientific context. In addition, members of SPIDVAC participated in various conferences and presented their work on AHS, PPR and FMD. But not only these three animal diseases kept us busy in recent months! At the beginning of September, a new bluetongue virus appeared in the Netherlands and our partners at Wageningen BioVeterinary Research sprang into action. Shortly afterwards, cases were also detected in Belgium and Germany, while epizootic hemorrhagic disease virus, which is related to the bluetongue virus, appeared in the south of France. As both diseases are transmitted by biting midges, it will be exciting to see how the situation develops when spring arrives.

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

News about notifiable animal diseases / Looking beyond the horizon

Current bluetongue situation in Germany

Dr. Jörn Gethmann, Dr. Bernd Hoffmann, Prof. Dr. Martin Beer, Prof. Dr. Carola Sauter-Louis FLI, Institute of Epidemiology and Institute of Diagnostic Virology

The notifiable animal disease bluetongue (BT) is making an impressive comeback with a massive outbreak in the Netherlands and an increasing number of cases in Belgium and Germany.

Bluetongue virus (BTV), like African horse sickness virus (AHSV), is a member of the *Sedoreoviridae* family (Genus Orbivirus). BTV is transmitted by biting midges and causes an acute disease in ruminants with a lack of appetite, apathy, high fever, salivation, swelling of the head, tongue and lips, reddened mucous membranes and coronitis with lameness. Infection with foot-and-mouth disease virus is a differential diagnosis that must be ruled out.

On September 3 and 4, 2023, Dutch veterinarians observed clinical signs of BT in sheep on five farms in the provinces of North Holland and Utrecht. Some of the affected sheep showed high fever (up to 42°C), swollen tongues, lesions in the mouth and on the tongue, reluctance to eat, salivation, and lethargic to moribund behavior. In addition, numerous sheep deaths were reported in the Netherlands. One day later, the Dutch reference laboratory for BT (WBVR)

confirmed the disease in four of the five farms and identified it as serotype 3 (BTV-3). By October 26, 2023, more than 2,000 holdings were affected, mainly sheep farms (Emergence of bluetongue virus serotype 3 in the Netherlands in September 2023; M. Holwerda et. al, <u>https://doi.org/10.1101/2023.09.29.560138</u>). The Dutch government initiated measures such as the closure of the affected farms and outbreak investigations.

On October 12, 2023, the first case of BTV-3 infection was detected in Germany. It occurred on a sheep farm in the district of Kleve, North Rhine-Westphalia (NRW). Since then, there has been another outbreak in NRW and an outbreak in

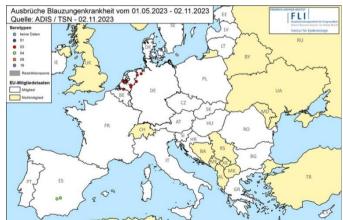


Figure 1 Map: Overview of cases of bluetongue since 01.05.2023, as of 02.11.2023

Lower Saxony. There is currently no vaccine against BTV-3 available in Europe, which means that animals cannot be effectively protected against infection. Germany had only been officially declared free of BTV on June 01, 2023, but restrictions and further spread are now expected to last beyond 2023.

Author: S. Weber

Access and Benefit Sharing and African horse sickness vaccine development in the SPIDVAC project: Walk the walk

The Nagoya Protocol, an international agreement that establishes a legal framework for the fair and equitable sharing of benefits arising from the use of genetic resources, entered into force in October 2014. Under the Protocol, genetic resources may include virus strains that can be used for research and development of vaccines. To date (December 2023), 141 countries have ratified the Nagoya Protocol, while not all countries have implemented the corresponding principles into national legislation.

One of the objectives of the SPIDVAC project is to develop innovative vaccines against African horse sickness (AHS). AHS is a devastating disease of equids caused by African horse sickness virus (AHSV), an arbovirus of the *Sedoreoviridae* family, genus Orbivirus. The infection of horses with AHSV leads to acute disease characterized by severe respiratory and circulatory impairment and is often fatal. The virus is endemic to tropical and subtropical areas of Africa, but it has repeatedly spread from its African habitat during the last century, causing severe outbreaks in Europe and most recently as far afield as Thailand, emphasizing that it is a continuous global threat to animal health and the horse industry. Safe and efficacious vaccines for AHS would directly benefit endemic countries such as South Africa and would be a key control tool in areas at risk of introduction like Europe or Asia. In the SPIDVAC project, the development of vaccines for AHS requires accessing virus strains and sequence information from South Africa.

South Africa ratified the Nagoya Protocol in 2013 and became a Party on Oct 12, 2014, although the country already had national legislation in place to regulate the exploitation of biological resources much earlier. Specifically, the National Environmental Management Biodiversity Act (NEMBA), outlining the requirements of material transfer and benefit sharing agreements, was approved in 2004 and came into force on the Jan 1, 2006. Specific regulations and procedures were put in place in 2008 with the Bioprospecting, Access and Benefit Sharing (BABS) Regulations. The University of Pretoria is collaborating with the National Department of Environmental Affairs (DEA) in South Africa to follow the necessary steps to comply with Nagoya, NEMBA and BABS regulations. This will ensure the fair and equitable sharing of benefits arising from the use of AHSV-derived genetic resources in the SPIDVAC project.

Author: J. Kortekaas

5 Facts about AHS

- 1. African horse sickness (AHS) affects all members of the Equidae family including horses, mules, donkeys, and zebras and is spread by biting midges (vectorborne). It is not transmitted by direct contact between equids.
- 2. AHS is caused by a virus of the genus Orbivirus belonging to the family Sedoreoviridae. Together with bluetongue virus and epizootic hemorrhagic disease virus, AHS virus is one of the three economically most important orbiviruses.
- 3. The first major recorded orbivirus epidemic was caused by AHSV in 1719, killing 1,500 animals. AHSV was discovered to be a virus in 1900.

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- 4. The mortality rate in horses is generally between 50% and 90%, 50% in mules and 5% to 10% in European and Asian donkeys. African donkeys and zebras are the least susceptible equines and are considered to be reservoirs for the virus, because they can transmit the virus to vectors but do not usually get sick.
- 5. Attenuated (monovalent and polyvalent) vaccines of all serotypes, except serotype 5, are currently commercially available for use in horses, mules and donkeys in Africa. They are not used outside of Africa due to concerns about their safety and the inability to differentiate between infected animals and animals vaccinated with these live vaccines.

Author: S. Weber

3 Questions to...

Carolina dos Santos Ribeiro (Ethics Advisor)

- What opportunities do you see in the SPIDVAC project? Opportunity to learn more about how policies and laws impact scientific work and progress and to co-create creative bottom-up solutions for alleviating these challenges
- What is your favorite part of being a scientist in general? To be able to position myself independently, based on scientific evidence, and to cooperate with others passionate about the same topics
- How would you describe your role as an External Independent Ethics Advisor within SPIDVAC?

My role is to, from an external expert view, give input on what I believe to be opportunities and challenges for the Consortium, and use my expertise to advise on potential ways to handle such challenges



• What opportunities do you see in the SPIDVAC Project?

Even if nowadays I am not as much immersed in infectious disease research as I have been for the last decades, I remain convinced that emerging animal diseases are a major research theme for the veterinary field in a "one health" world as recent pandemics have proven. As a consequence, reinforcing the abilities of developing new vaccines in a timespan which makes it compatible with control of epizootics before they get a chance to become epidemics is a major asset. This does not reduce the time of administrative approvals, but building a European network of researchers remains an improvement on the scientific side.

• What is your favorite part of being a scientist in general?

I see three major axes in which I am experiencing pleasure at working around scientific research: (a) improving my knowledge, (b) tracking questions in the field I am working for and (c) building experimental protocols to (try and) answer these questions. And then, as in much human activities, meeting persons with whom I share interests.

• How would you describe your role as an External Independent Ethics Advisor within SPIDVAC?

Probably the hardest question here. I mean, as the last meeting outlined, there are two very different ethical question groups. The simplest of these for a veterinarian like me is evaluating the impact on animals of the experimental procedures (in terms of wellbeing, number of individuals, experimental design and chances of success but also on



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usefulness of the produced results). Even on these questions there are parts which are impossible to answer before doing the work (especially on the chances of success) and I take for the role of the ethical advisor to outline for the researchers the risks of an unethical cost of the assays. One of the difficulties is of course the differences of the local regulations which could, for instance, make a standard assay done in some country definitively unacceptable in another. On these difficulties I guess there are no experts, so it has to be discussed between the teams. The other group of ethical questions is the impact of the research or its results on human society be it as a consequence of economic changes or by evolution of biological risks, and these are parts of ethics I cannot assess properly enough to give advice or even ask questions....

Who is Who? – PhD students/junior scientists introduce themselves

Kieran

Hi, I'm Kieran Pitchers and I am a research fellow with the SPIDVAC project. I started my scientific journey here at the University of Nottingham (UoN) 10 years ago now with a BSc, and besides one year working in Oxford, have remained at UoN completing my PhD and subsequent research opportunities. My PhD was focused on developing alternative therapies to antibiotics, with antimicrobial resistance a looming threat. My work after this has centered around developing diagnostics for veterinary pathogens and it is this experience, along with green-fingered protein expression in plants, I am excited to be using with this collaborative project.



Diana

Hello!

My name is Diana Dakik and I am a SPIDVAC postdoctoral researcher based in the UK at the University of Surrey. I came to the UK from Zambia almost 10 years ago to undertake my bachelor's degree in Veterinary Biosciences and then went on to undertake my PhD in Equine Immunology. My PhD was primarily to characterize the dendritic cells in the blood using various applications - my favorite being flow cytometry and single cell RNA sequencing. A big motivator for joining the SPIDVAC project was the opportunity to directly contribute to African Horse Sickness research which largely impacts my home region and my sport. I'm excited to bring my immunological skills and previous experience working in containment facilities on various animal studies. Looking forward to learning from and learning with all our international colleagues!



Working international - Introducing the project partners -PARTNER FOCUS: INNOVATIVE DIAGNOSTICS

<u>IDvet - Innovative Diagnostics</u> is honored to be a member of the SPIDVAC consortium.

Loïc COMTET, our Livestock R&D and Global Range Manager, is co-leading with Emmanuel Bréard from the French Agency for Food, Environmental and Occupational Health & Safety (ANSES) the Work Package dedicated to diagnostics. He is also a member of the Executive Board, while Alix Carpentier, our Equine R&D Manager, is in the Steering Committee of the project.

Diagnostic specialists from our Livestock (Loïc Comtet and Fabien Donnet) and Equine (Alix Carpentier & Océane Mercier) units are committed to bringing their knowledge and expertise to the development of new DIVA tests for PPRV, AHSV and FMDV.

OUR COMMITMENT TO THE ONE HEALTH CONCEPT



Our company has always been acting for *One Health*: as veterinary diagnostics specialists, we know that the health of people is intimately connected to the health of animals and the environment, especially in this age of globalization. We help to protect both human health and the global food supply by offering diagnostic tests to detect zoonotic diseases in humans and animals, and veterinary diseases in farm animals.

Our tests, mainly based on ELISA and qPCR techniques, are used worldwide to:

- Control veterinary diseases
- Detect emerging and re-emerging diseases
- Limit disease spread when animals are moved between farms and countries
- Detect zoonotic diseases, transmissible to humans
- Verify the effectiveness of vaccination.

Innovative Diagnostics strives to be at the cutting edge of veterinary diagnostics thanks to inhouse technical expertise, high throughput production and close relationships with leading scientists worldwide.

IN-HOUSE TECHNICAL EXPERTISE



The key feature of the Innovative Diagnostics production workflow is that we manage the entire process on site from raw biological materials (monoclonal antibodies, recombinant proteins, viral and bacterial antigens) through to final product.

This enables us to take a hands-on approach to quality at every step and offers us flexibility. In turn this means we can maintain a customer-orientated outlook to our business, offering a bespoke service where possible.

HIGH THROUGHPUT IN MANUFACTURING

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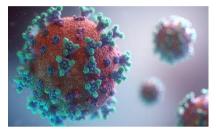
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Highly skilled staff and modern infrastructure allow Innovative Diagnostics to guarantee the production of high volumes of biological components, ELISA and PCR reagents, with rapid delivery around the world.

QUICKLY REACTING TO SANITARY EMERGENCIES

Innovative Diagnostics is a science-driven company, investing 30% of profits in Research and Development activities. Independently owned, the company can rapidly develop diagnostic solutions to new outbreaks.



For example, we developed the first Schmallenberg virus ELISA worldwide after an outbreak in Europe in 2011.

More recently, Innovative Diagnostics was able to quickly react to the emergence of the SARS-CoV-2 virus offering a complete diagnostic range: in April 2020, the company was the first in France to offer a serological test.

EXTENSIVE EXPERIENCE AS AN INDUSTRIAL PARTNER IN INTERNATIONAL PROJECTS



Since its creation in 2004, Innovative Diagnostics has been an active partner in a number of European funded collaborative projects (H2020, H2021), contributing development of specific ELISAs, providing prototypes to all partners and/or participating in the organization of experimental studies and ring trials.

In addition to SPIDVAC, Innovative Diagnostics had been involved in DEFEND (covering ASFV and LSDV), PARATBTOOLS (2006-2012), EDENext (CCHFV), ORBIVAC (BTV, EHDV and AHSV), FLUAID (AIV) projects.

WIDE RANGE OF TESTS FOR THE DETECTION OF PPRV AND FMDV

Our tests for PPRV detection currently include:

- ID Gene[™] Peste des Petits Ruminants Duplex qPCR
- ID Rapid® PPR Antigen rapid test
- ID Screen® PPR Antigen Capture ELISA
- ID Screen® PPR Competition ELISA

Our tests for FMDV detection currently include:

- ID Screen® FMD NSP Competition ELISA
- ID Screen® FMD Type Asia1 Competition ELISA
- ID Screen® FMD Type O Competition ELISA

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UPCOMING TEST FOR THE DETECTION OF AHSV

An ELISA test for the detection of African Horse Sickness Virus VP7 is currently under development.

KEY FACTS ABOUT IDVET-INNOVATIVE DIAGNOSTICS



- Company founded in 2004
- Our diagnostic solutions:
- include ELISA, qPCR and rapid antigen tests

• **cover more than 50 veterinary diseases** including PPR and FMD, as well as **zoonotic diseases** like CCHF, Q Fever, West Nile Fever, Rift Valley Fever, Glanders and COVID-19

- 5000 m² facilities located near Montpellier, France
- Offices in Brazil, Jordan, India, China
- 170+ employees

• Independent and 100% self-financed company: our own R&D activities and state-of-the art, automated production line allows us to react immediately to sanitary emergencies

• Certified ISO 9001:2015

Website: https://www.innovative-diagnostics.com/

Authors: L. Comtet, A. Barthes, A. Carpentier

SPIDVAC annual Meeting in Paris 2023

After the kick-off meeting for the SPIDVAC project launch in September 2022 took place online, the entire consortium was finally able to meet in person at ANSES in Maisons-Alfort, France, for the 2023 annual meeting. This included all 13 consortium partners from Europe and Africa, as well as the members of the Scientific Advisory Board and the Ethics Committee. For two days, the École nationale vétérinaire d'Alfort offered us a discussion forum for progress and results, collegial talks and collaborations. The workshop for young scientists was also a success. The

young colleagues not only got to know each other better, but also found a platform to discuss problems and make new contacts. They were also able to present their work to the project partners. In addition to the scientific topics, socializing was not neglected. We enjoyed a very informative tour of the Île de la Cité and the famous Notre-Dame de Paris cathedral and then rounded off the first meeting day with a nice dinner in a relaxed atmosphere.



Author: S. Weber Picture: M. Eschbaumer

Outside the Lab - SPIDVAC goes to meetings

Madrid. The workshop of the European reference laboratory on Bluetongue and African Horse Sickness (AHS) (Laboratorio Central de Veterinaria, Algete, Spain) was organized on the 7 and 8 of November in Madrid. Ewa Camara from the EU Commission was present and three partners of the SPIDVAC project attended this meeting: Javier Ortego and Eva Calvo-Pinilla from CISA-INIA/CSIC, Piet Van Rijn and Melle Holwerda from Wagenigen BioVeterinary Research, Corinne Sailleau, Damien Vitour, Emmanuel Bréard and Stéphan Zientara from ANSES. About 40-45 participants of the EU Member States (but also from South Africa and Nigeria) attended this meeting. Javier Ortego presented the IFNAR^{-/-} mouse model to assess the efficacy of vaccines against AHS. Stéphan Zientara presented the SPIDVAC project and in particular the development of AHS vaccines and companion tests. Piet Van Rijn presented the approach of the DISA vaccine against AHS.

This meeting was a perfect occasion to inform the scientific community involved with AHS diagnosis about the SPIDVAC project.

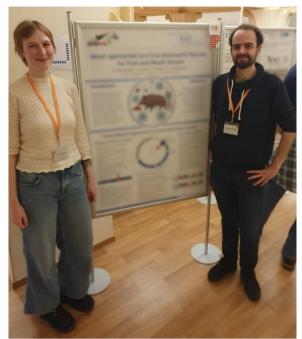
Author: S. Zientara

Prague. The FEEVA (Federation of European Equine Veterinary Association) has invited Stéphan Zientara to give a talk on the vaccines against AHS in Prague on the 27 of September. On this occasion, Prof Zientara has taken the opportunity to present the SPIDVAC project. The EU Commission was represented by Dr Ewa Camara and the WOAH by Dr Mauro Meske.

Author: S. Zientara

Jena. From November 15 to 17, 2023, this year's Junior Scientist Symposium (JSS) with the theme "One Health & Emerging Pathogens: Current and Upcoming Strategies in Science" took place at the FLI site in Jena. The JSS is a symposium initiated by the FLI and organized by and for FLI PhD students. In addition to the diverse contributions from young scientists, the program was enriched by exciting keynote lectures on One Health, antibiotic resistance and Open Science.

Of course, the two SPIDVAC doctoral students from the FLI were also in attendance. While Constantin Lorenz provided the audience with insights into the project and its overall objectives, Kira Wisnewski, through her poster presentation, informed participants about various ways to develop an attenuated live vaccine for Foot-and-Mouth Disease.



Picture: private; Author: S. Weber