

A photograph of a wooden crate filled with dry grass and straw. A white plastic bag is visible in the background. The text "ECO-SYSTEMS" is overlaid on the image.

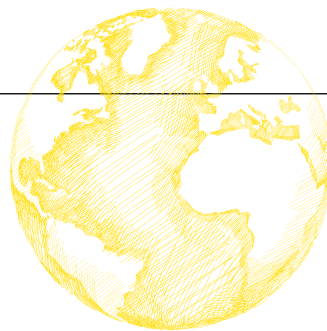
ECO-SYSTEMS



Getting a head start on health threats

3

Dedicated to “One Health” ↘



ANSES’s scope of action covers health threats to humans, animals and plants. In a world where borders are blurring and unprecedented new threats are emerging, such as the COVID-19 pandemic, the Agency reaffirms its commitment to European and international “One Health” scientific co-operation. The aim is to increase the alert and action capabilities of health authorities worldwide.

With expertise in human, animal and plant health, it is only natural that ANSES adopts a cross-cutting approach to health issues. As all living organisms and ecosystems are interconnected, the Agency can plainly see how closely the health of some depends on the health of others, and how they are all suffering the health consequences of the globalisation of trade and global warming. This is why ANSES is guided by the “One Health” principle – an integrated, holistic approach to health – as set out in the various national, European and international action plans in which the Agency is involved.

As part of the European Commission’s Horizon 2020 programme, since January 2018 ANSES has been coordinating the “One Health” European Joint Programme (EJP), which seeks

to build a genuine European research area for foodborne zoonoses, antimicrobial resistance and emerging risks. Because a global perspective is needed now more than ever before to anticipate new threats, the Agency has also been taking part in the recent MOOD project to develop innovative tools for health monitoring and early detection of warning signals. In particular, it has contributed its expertise on antibiotic-resistant bacteria in the animal world, a subject on which it also actively promotes broad and reinforced surveillance of animal exposure to these bacteria. The RESAPATH network, which it coordinates, is the only monitoring scheme on this subject in the European Union. ANSES is also heavily involved in three fields of health risks where a holistic view is necessary: vector-borne

diseases transmitted in particular by mosquitoes, ticks and phloem-feeding insects; bee health; and the interface between wildlife and domestic animals, which plays a crucial role in the emergence or resurgence of many animal and human diseases. In 2019, the Agency actively contributed to improving the scientific benchmarks mobilised to combat the spread of bovine tuberculosis by badgers, or of African swine fever by contaminated wild boars at the Belgian border. It also helped advance knowledge on the modes of transmission and circulation of Lyme disease in our country. Lastly, ANSES is an international reference laboratory for several diseases transmitted by wildlife, such as rabies and bovine tuberculosis.

THE “ONE HEALTH” EUROPEAN JOINT PROGRAMME (EJP)

This programme, coordinated by ANSES, brings together more than 40 partners from 19 Member States, including the MED-VET-NET network of excellence on foodborne zoonoses. It supports scientific research on micro-organisms and contaminants that affect human health, animal health and the environment, particularly through food. Besides ANSES, the other French partners of the “One Health” EJP are INRAE, the *Institut Pasteur* and *Santé publique France*. Launched in January 2018 for five years, it has a budget of €90 million provided by the European Commission and the Member States.

Its objectives are to:

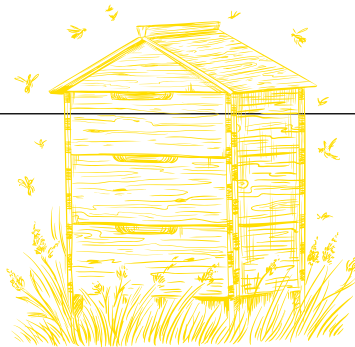
- fund research projects in the areas of foodborne zoonoses, antimicrobial resistance and emerging risks;
- generate scientific data to be used as input for the analysis and assessment of health risks by national and European agencies;
- bring public and veterinary health agencies closer together and ensure the effective dissemination of information within the scientific community.

ANSES's laboratories responded to the second call for research projects in 2019 and are participating in 12 new partnership programmes with a total budget of €3.5 million. These activities were highlighted at the first annual scientific meeting of the “One Health” EJP in Dublin in May 2019, an event that consolidated the foundations of the project's scientific community. This joint programme is also a powerful tool for responding to health crises: in early 2020, it set up a “Joint Integrative Project” to organise its members' response to the SARS CoV 2 crisis.

MOOD: RETHINKING GLOBAL HEALTH MONITORING TO ADDRESS EMERGING DISEASES

→ The European MOOD project – MOnitoring Outbreak events for Disease surveillance in a data science context – aims to unify and strengthen health monitoring systems. Improving epidemic intelligence tools and services could, in particular, enable earlier identification of the risk of introduction and spread of a new pathogen, and of the areas favourable to its spread. Coordinated by CIRAD as part of the European Horizon 2020 programme, MOOD has a budget of €14 million and brings together 25 research institutions, public health agencies and veterinary services from 12 countries. When it comes to an end in late 2023, its participants will have developed new monitoring tools to complement existing ones, for sharing by all countries. The epidemiologists of ANSES's Lyon Laboratory are contributing to this project.

Protecting bee health



Diseases, predatory insects, pollen depletion, pesticides... ever since it was founded, ANSES has been studying and assessing co-exposure to stress factors that threaten bees, and proposing scientific and regulatory solutions to protect their health. Its Sophia-Antipolis Laboratory has established itself as a national and international reference in the field.

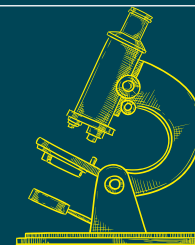
Pollinating insects are essential to the reproduction of many plants. Honeybees and wild bees, which together account for 90% of these insects, are affected by a worrying worldwide phenomenon of excess mortality that threatens plant diversity and the food supply. Since its creation, the Agency has been particularly active on this subject, with a global approach to risk factors that takes no account of national borders.

Among other things, the Agency has distinguished itself by highlighting the multifactorial nature of bee colony collapse, showing a complex situation of interactions between pathogens, parasites such as *Varroa*, and chemicals. Some of these chemicals, particularly insecticides of the neonicotinoid family, reduce the bees' immune defences and make them more susceptible to pathogens. They also inhibit their detoxification abilities, and interfere with their orientation and communication.

These stress factors are compounded by declining food resources due to the loss of biodiversity, especially in the flowers most prized by bees, and climate change. In view of these findings, ANSES has recommended several avenues of work to be explored, such as the development of improved multi-residue measurements on bee specimens and hive products to better identify the molecules found in the insect's environment, and the creation of a network of reference apiaries to better analyse the situation of colonies in the different regions. The Agency has also recommended strengthening requirements for the protection of bees and other pollinators in the preparation of marketing authorisation applications, and restricting the use of certain plant protection products in order to limit their contact with pollinating insects.



ANSES's recommendations on reducing bee exposure to plant protection products



→ Systematic assessment of acute and chronic risks to adult bees, larvae and bumble bees in the context of product marketing authorisation applications.

→ No application of any products — not just insecticides — during periods when crops are attractive to bees and other pollinating insects.

→ In the studies to be carried out for marketing authorisations, better assessment of long-term risks to bees and other pollinators, including the introduction of measurement of the time taken to return to the hive.



10 YEARS OF EXPERT APPRAISALS ON BEE HEALTH

2011

→ The Sophia-Antipolis Laboratory, which has been in operation for more than 40 years, was named European Union Reference Laboratory for bee health.

2014

→ The Sophia-Antipolis Laboratory contributed to the European SmartBees project, focused on the natural resistance of bees to the major parasite *Varroa destructor*.

2018

→ Recommendations to strengthen national provisions imposing restrictions on the use of plant protection products during periods when crops are attractive to these insects.

BETWEEN 2012 AND 2015

→ ANSES conducted an expert appraisal on the effects of co-exposure of bees to various stress factors and their respective role in colony weakening, collapse or mortality phenomena.

2015

→ Expert appraisal on the ranking of bee diseases.

2016

→ Expert appraisal on the risks of insecticides containing substances from the neonicotinoid family.

2018

→ The Sophia-Antipolis Laboratory contributed to the European PoshBee project to quantify the pesticide hazard for bees.

2019

→ Recommendations to improve risk assessment methods in the framework of marketing authorisation applications for plant protection products.

2019

→ ANSES and the European Food Safety Authority (EFSA) organised an international scientific conference in Paris on bee health and how research can contribute.

2011

➤ TEN YEARS OF ANSES,
see our selected highlights
on www.anses.fr/en

2019

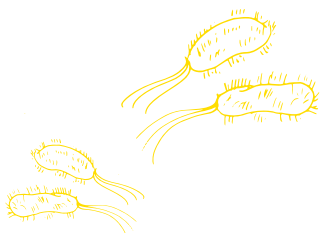
Combating bacterial resistance to antibiotics ↘



Animal health is one of ANSES's areas of excellence, supported by its research laboratories and, within its Regulated Products Assessment Department, by the French Agency for Veterinary Medicinal Products (ANMV).

At the crossroads of their activities, the use of antibiotics on farms, the selection of resistant bacteria and their consequences for human health are a subject where vigilance is still required, despite the progress observed.

ANSES is the National Reference Laboratory for antimicrobial resistance, and as such it monitors bacterial resistance in the food chain as part of surveillance plans that have been harmonised at European level. For its part, the ANMV grants marketing authorisations for veterinary antibiotics in France and monitors their use and effectiveness under actual conditions of use, taking into account the particular risk of selection of resistant bacteria.



In November 2019, to mark World Antibiotic Awareness Week and European Antibiotic Awareness Day, ANSES published three reports reviewing the situation regarding antimicrobial resistance in animal health in 2018:

→ The first report was its sales survey of veterinary medicines containing antimicrobials in France, based on sales data from the ANMV and one-off surveys on livestock farms carried out by ANSES laboratories, which provided descriptive data on the prescription and use of antibiotics.

→ The second report consolidated the findings of RESAPATH, the French Surveillance Network for Antimicrobial Resistance in Pathogenic Bacteria of Animal Origin. Coordinated by ANSES, RESAPATH is the only surveillance network of its kind in Europe.

→ The third report focused on post-marketing authorisation surveillance of veterinary medicinal products, including the monitoring of adverse effects reported by the pharmacovigilance scheme for veterinary medicinal products run by ANSES.

These reports' main findings are encouraging: since 2011, exposure to antibiotics for all animal species combined has decreased overall by 38.4% and the volume of sales of veterinary antimicrobials has fallen by 48%. Efforts for the prudent and responsible use of antimicrobials in veterinary medicine must however continue. ANSES's data on antimicrobial resistance are used to assess the effectiveness of public policies on antibiotic use, in line with the 2016 interministerial roadmap to control antimicrobial resistance by taking human, animal and environmental health into account according to the "One Health" approach.

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VETERINARY MEDICINAL PRODUCTS: ACTIVE PARTICIPATION IN IMPLEMENTING THE NEW EUROPEAN REGULATIONS

→ New EU regulations for veterinary medicinal products and medicated feeds came into force in January 2019. Their implementation will require numerous delegated and implementing acts. In order to prepare these, the European Commission mandated the European Medicines Agency (EMA) to provide scientific and technical opinions. The ANMV experts within ANSES

have been heavily involved in the working groups set up by the European agency, holding several chairs and co-chairs. In particular, they have been working to define criteria for drawing up the list of antibiotic substances to be reserved for human medicine, and the arrangements for collecting data on the sale and use of antimicrobial drugs used in veterinary medicine at Euro-

pean level. Concerning the establishment of a common database of veterinary medicinal products in the European Union, an expert group chaired by the Deputy Director of the ANMV made recommendations in late August 2019 to set up a reference database that is interconnected with other European databases and tools.

Preserving the health of plants and ecosystems ↘



The plants populating our natural and cultivated areas face threats that are continually evolving. Climate change and human activities are altering ecosystems and promoting the emergence or re-emergence of diseases and pests. International trade is increasing and can also accelerate the introduction of pests from neighbouring or distant countries. The Plant Health Laboratory helps prevent health crises and protect our plant heritage and crops. It saw a number of major events in 2019.

AVOID CONFUSING EDIBLE PLANTS WITH TOXIC PLANTS

→ Some toxic plants (such as horse chestnut or lily of the valley) resemble edible plants, and may be confused with them not only in the wild, but also in the garden or vegetable patch. Two hundred and fifty cases of confusion are documented by the French poison control centres every year. ANSES, which coordinates the national toxicovigilance scheme and the activities of the poison control centres in this area, reviewed these poisonings and called for greater vigilance with regard to such cases of mistaken identity.

↘ Find out more on www.anses.fr/en

XYLELLA FASTIDIOSA, A THREAT TO OUR OLIVE TREES

The *Xylella fastidiosa* bacterium threatens more than 500 plant species, including grapevines, almond, citrus, oak, coffee and especially olive trees. Transmitted by insect vectors that feed on sap (xylem), it causes infected plants to dry out. After the disease arrived in France in 2015, a surveillance plan was put in place to prevent its spread. If detected, any infected plant is destroyed. The Plant Health Laboratory is the National Reference Laboratory for identification and detection of the bacterium. Since 2015, 48,000 samples taken from ornamental, wild, aromatic or cultivated plants have been analysed by the specialised unit in Angers. In Montpellier, the Pests and

Invasive Plants Unit identifies insect vectors of the disease, such as meadow spittlebugs, a members of the leafhopper family. In 2019, ANSES confirmed the presence of *Xylella fastidiosa* on two olive trees in the Provence-Alpes-Côte d'Azur region. Scientists were able to determine that one was contaminated with subspecies *pauca* and the other with subspecies *multplex*. This discovery led to the introduction of enhanced surveillance measures, the only way to combat this disease. Along with INRAE and EFSA, ANSES co-organised a scientific symposium on the subject, which brought together more than 300 participants in Ajaccio.

PHILIPPE REIGNAULT, DIRECTOR OF THE PLANT HEALTH LABORATORY

"The Plant Health Laboratory plays a major role in hazard detection and risk assessment thanks to more than 40 years of experience, scientists with rare expertise in mycology, entomology, virology, national and European reference mandates for all pests, state-of-the-art technologies and a unique quarantine system. Together with the Lyon Laboratory, which studies phenomena of resistance to plant protection products and is involved in monitoring outbreaks, ANSES has a coherent whole, capable of advancing science to keep pace with the changes observed. This means producing ever more comprehensive scientific knowledge, developing yet more effective detection and identification methods, and acting in synergy at European and international level, in order to remain vigilant and ready to tackle threats and emerging phenomena, which are today global and diverse."



HIGH ALERT FOR PINE TREES AND TOMATOES

The pinewood nematode *Bursaphelenchus xylophilus* on the doorstep of the Landes forest

A microscopic worm responsible for significant dieback in conifers, the pinewood nematode poses an imminent threat to forests of maritime pine in France. Currently found in Portugal and Spain, it could contaminate the Landes area. Following the interception of bark and wood packaging containing the nematode, ANSES conducted several expert appraisals to assess the risk of the pest's entry and spread in France. The Agency immediately made recommendations on the use of wood and bark likely to be affected.

Alert regarding Tomato brown rugose fruit virus (ToBRFV)

ANSES also worked to tackle a new emerging virus threatening tomato, chilli pepper and sweet pepper crops in France. Simple physical contact with a diseased plant is enough to contaminate a healthy plant. The virus can also survive in the open air for several weeks or even months without losing its infectivity. There is currently no treatment, and no variety is resistant to this virus. In its expert appraisal, ANSES warned of the high risks of introduction of the virus and reiterated the importance of the measures to be adopted to prevent its spread across France. The Plant Health Laboratory conducted the analytical tests that confirmed the case of contamination in Finistère.

Our laboratories, risk watchdogs ↘

Always on the lookout for recurring and emerging health risks, the ANSES laboratories explore threats and help combat them in three areas of key importance: animal health and welfare, plant health and food safety.

Besides their contribution to the Agency's expert appraisals of health issues, they conduct scientific research, often in partnership with French and international research organisations, and design ever more powerful detection and identification technologies that improve understanding of both the spread of pathogens and their interactions with hosts. They hold numerous reference mandates, and help public authorities monitor, prevent and manage health crises in France or beyond our borders.

In 2019, ANSES obtained three of the five new reference mandates in plant health introduced by the European Commission. These cover fungi and oomycetes, insects and mites (with the Austrian

agency AGES), and nematodes (with the Belgian institute ILVO). For the latter two, ANSES is in charge of managing the consortia formed. These were the very first European mandates established for plant pests.

At the same time, ANSES took the helm of a new reference centre for animal welfare. In late 2019, it was appointed to lead the new European Reference Centre for the welfare of poultry and other small farmed animals, together with its partner organisations in Spain, Italy and Denmark. The objective is to improve husbandry conditions at all key stages in the animals' lives: from birth or hatching through to slaughter or end of life.

WHAT DO WE MEAN BY REFERENCE?

→ For certain pathogens or chemical contaminants of major importance, the health authorities set up specific surveillance schemes. At the national level, for each theme, State services approve a network of field laboratories to carry out official analyses, and appoint a "National Reference Laboratory" (NRL), whose role is to guarantee the reliability of the analyses carried out and

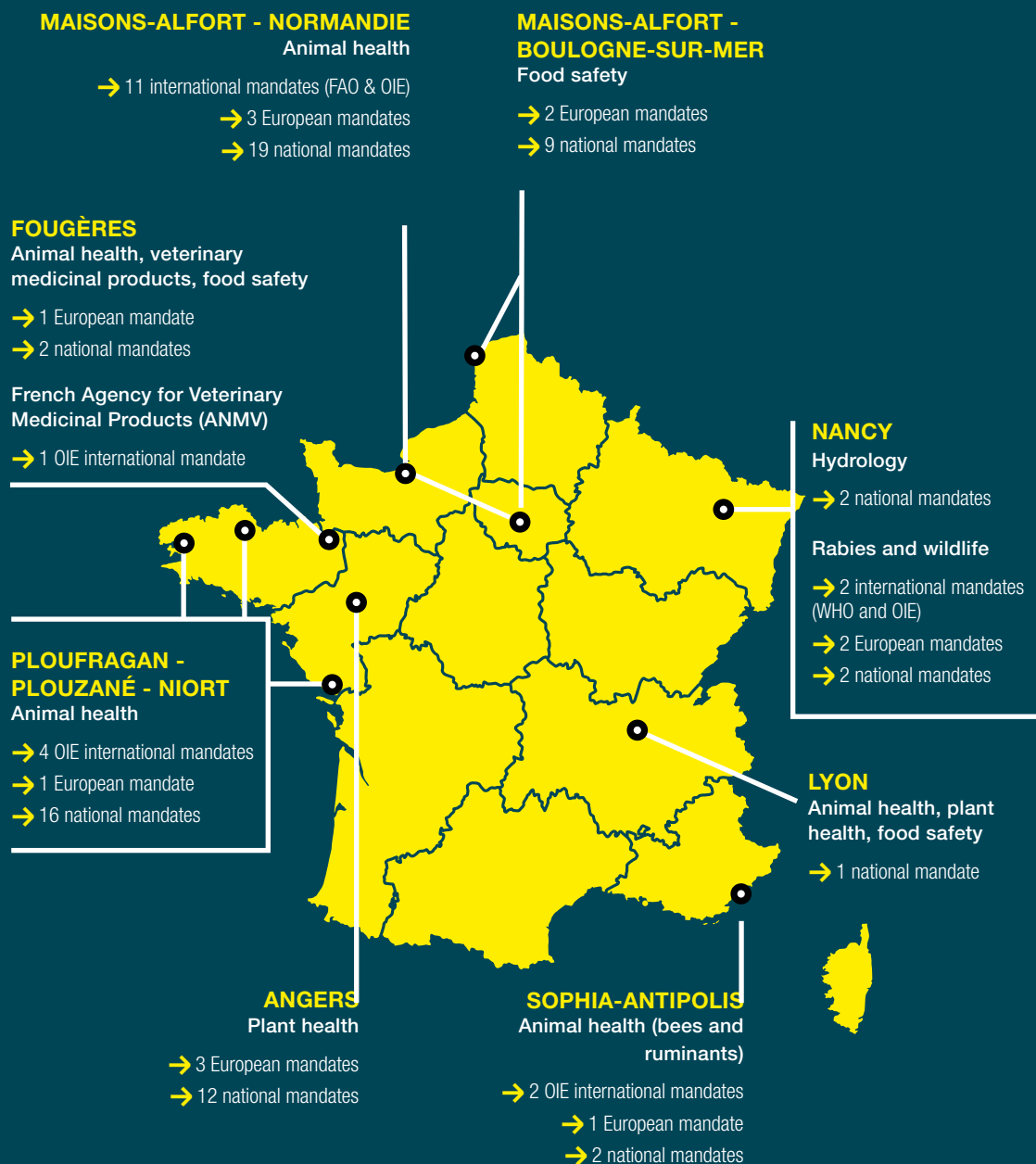
to manage the network of laboratories.

→ The schemes in each country are supplemented and coordinated at European and international level. For example, the European Commission appoints "European Union Reference Laboratories" (EURLs) to run the network of National Reference Laboratories on the same topic. Meanwhile, at the

international level, the World Organisation for Animal Health (OIE), the World Health Organization (WHO) and the Food and Agriculture Organization of the United Nations (FAO) appoint reference laboratories, reference centres or collaborating centres to provide the necessary technical assistance to these organisations and to Member States.

Reference mandates

→ At end 2019, ANSES held 65 national reference mandates, 13 European mandates and 28 international mandates including:



GILLES SALVAT, MANAGING DIRECTOR GENERAL OF THE RESEARCH AND REFERENCE DIVISION



CROSS-CUTTING LINKS

"Our scientific skills and the co-operation between teams give us a broad vision of the issues at stake, which is needed to answer increasingly complex questions. For example, a unit of ANSES's Laboratory for Animal Health worked with the French Agency for Veterinary Medicines on the resistance of certain cattle parasites to antiparasitic compounds, and on the release of these products into the environment with possible impacts on bee health. This has led us to consider alternative control concepts and review animal husbandry conditions, which then also responds to societal demand for more ecological solutions and improved animal welfare."

OUR SCIENTIFIC DYNAMISM IN FIGURES

394 ANSES
scientific publications
in international
peer-reviewed journals
(category A+ and A)
in 2019

A success rate
in competitive calls
for projects of
46%

58 foreign
scientists hosted in
our laboratories to carry
out activities as part of
scientific co-operations

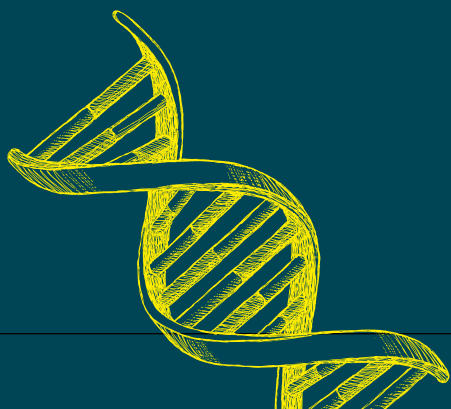
3 framework
agreements signed
in the past year, with:

- French Agricultural Research Centre for International Development (CIRAD);
- University of Rennes 1;
- University of Paris-Est Créteil

Focus

GENOMICS FOR IDENTIFYING FOOD PATHOGENS

ANSES is interested in cutting-edge research and diagnostic techniques, and particularly in the opportunities provided by genomics. In 2019, with its German, Danish and Korean counterparts, the Agency organised an international symposium on the impact of an approach that is becoming increasingly widespread: whole genome sequencing of foodborne pathogens, in order to explore and discuss international practices and partnerships, whether already established or to come. Last year, for example, this major technological leap helped identify genomic markers of the animal species that was the original host of *Campylobacter jejuni* (the bacterium that is the primary cause of food poisoning in France), and led to the discovery that in addition to poultry meat, consumption of undercooked beef was also a major source of food poisoning in France. This work, published in a leading international scientific journal, will in the future play an essential role in guiding prevention policies against this bacterium.



RESEARCH: FLAGSHIP PUBLICATIONS IN 2019

While support for public authorities is the priority for ANSES's laboratories through their monitoring and reference work, research is the basis of their activity. The work carried out covers the entire spectrum, from fundamental research through to methodological developments specific to applied research.

Our teams' scientific publications in 2019 perfectly illustrate this continuum. For example, they have led to improved methods for the detection of *Xylella fastidiosa* and of hepatitis E virus in foods, and the development of three-dimensional liver cell culture methods for use in toxicology models. Other teams have shown how the pandemic H1N1/2009 influenza virus passed from humans to pigs and then from pigs to humans, or the role of cleaning and disinfection practices in selection of antibiotic resistance genes in bacteria of the *Salmonella* genus.

In a more fundamental research field, several studies have furthered knowledge of the interactions between pathogens and their hosts or pathogens and their vectors, which will help improve techniques for combating the animal and human diseases transmitted by these pathogens. For example, modification of tick cell microRNAs by *Anaplasma phagocytophilum*, understanding of novel functions of the bluetongue virus NS3 protein in regulation of the MAPK/ERK intracellular signalling pathway, or the role of the α -synuclein protein in the expression of Parkinson's disease, are just some of the flagship publications in the broad field covered.