ANSES 2023 work programme

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I. General orientations

ANSES's 2023 work programme echoes the transition between the framework defined by its 2018–2022 goals and performance contract (COP) and the early stages of the 2023–2027 COP currently being negotiated between the Agency and its supervisory authorities. While it is consistent with both frameworks, the programme reflects more generally **a context deeply marked by unprecedented developments**.

Indeed, in the wake of the COVID-19 pandemic and in the face of other rising threats, the perception of the importance of a comprehensive approach to health – One Health – has never been so acute. This approach is a historic opportunity for ANSES, which was founded and operates on the principle of a comprehensive approach to risks at the intersection of the three pillars of the One Health concept: animals – humans – environment.

Moreover, the notions of sustainability, durability and climate change impact have gone from being somewhat intangible concepts to concrete realities for a large part of the population and society stakeholders. Tensions over water, energy and certain commodities (food, manufactured goods such as semiconductors) are being clearly felt and have been exacerbated by particularly acute climate events (intense heat, prolonged drought, high-intensity hazards). This manifestation in everyday life is a strong driver for greater individual and collective awareness and action. Knowledge of risks is therefore needed more than ever, so that these growing concerns can be focused on the deeper issues of environmental and health questions and be addressed together under the auspices of this global health.

At the same time, growing awareness about the consequences and costs of resolving risks – whether health or environmental – is leading to public policies on health and risk, taking greater account of prevention and its prerequisite of adequate information on the risk factors to be prevented or controlled. The scale of the COVID-19 pandemic has also generated new and sometimes contradictory expectations in terms of protection, guidelines, rules and information, which require the various public players – including ANSES – to rethink how they contribute to managing crisis situations. In particular, there are high expectations that ANSES will be able to identify the potential sources of the next situation likely to exceed the collective response capability.

Furthermore, **the Agency's orientations translate Europe's strategic challenges at its own level**. These include the European Green Deal and the resulting actions and strategies, such as the Farm to Fork Strategy for a healthier and more sustainable EU food system, the EU's Biodiversity Strategy for 2030, the Chemicals Strategy for Sustainability, and the Action Plan for the development of EU organic production. ANSES's work is also in line with the European Action Plan against Antimicrobial Resistance, the Pharmaceutical Strategy for Europe, and Europe's Beating Cancer Plan, as part of the EU's health programme (EU4Health).

Faced with this context and within its missions, **ANSES's response is built around three main themes**:

- pursue and amplify the Agency's know-how, which in some cases has long echoed these challenges;
- increase vigilance, in particular by interlinking schemes and data, and foster anticipation through research and emergency preparedness;
- develop our contributions to foster and support the needs of transitions, for all risk governance players.

Pursuing and amplifying know-how means first of all multiplying those of ANSES's actions that put the One Health concept into practice, making them clearer and pushing them further.

At the intersection between the One Health concept and the exposome approach, for which our Scientific Board has just finalised a report and a roadmap, the aim is to further analyse the interactions between risk factors of all kinds: pathogens, hosts (wild/domestic animals, animals/humans), environments, contaminants, etc. The Agency should aim to identify which of these interactions have significant effects and impacts, and in particular which lead to greater effects than can be addressed by the usual risk assessment approaches.

Similarly, the question of multiple exposure can only be addressed by combining analyses of work-related situations in the context of occupational health with those of personal life situations that have more to do with an environmental health approach. A major issue such as the impact of dust/particles should be investigated as a whole.

Lastly, the Agency must ensure that it cultivates the areas in which it is at the forefront **in France and Europe**, in terms of research, reference and risk assessment. It is in a position to play a leading role in the following areas: assessment of chemicals with regard to the endocrine disruption hazard, development of advanced methods for assessing complex exposures, assessing the risks associated with substances in nanoscale form, work on antimicrobial resistance, analysing the ability of pathogens to cross species barriers. It is also a European Reference Laboratory in many areas of animal health, food safety and plant health, and a European Reference Centre for animal welfare.

Increasing vigilance and fostering anticipation means first of all working to interlink vigilance, surveillance and data analysis systems. Firstly, maintaining close cooperation between national reference laboratories (in animal health) and national reference centres (in human health) is essential to identify the possible evolution of an animal epidemic – such as highly pathogenic avian influenza – into a zoonotic disease that can be transmitted to/by humans. ANSES addresses the early detection of emerging threats in the different areas of its work through rapprochement or cooperation between schemes, whether in occupational health, antimicrobial resistance or on the subject of resistance to plant protection treatments.

Promoting monitoring and control policies that have been prioritised using risk analyses also contributes to more efficient vigilance, as does conducting advanced risk assessment work to identify windows of exposure or populations more vulnerable to certain risk factors.

Anticipation, the indispensable counterpart to vigilance, is also reflected at ANSES by the development of risk research activities in its laboratories and assessment departments, and through financial support for the National Research Programme for Environmental and Occupational Health (PNR EST) led by ANSES.

The scientific reputation and experience gained in major projects such as the European Partnership for the Assessment of Risks from Chemicals (PARC) have also led the Agency to volunteer its involvement in future European research partnerships of equivalent ambition in the areas of animal health and welfare, sustainability of future food systems, and antimicrobial resistance.

Lastly, fostering anticipation means preparing and planning for organisational modes geared to emergencies or planned large-scale situations such as major sporting events, including the 2024 Olympic Games, with a key challenge being to integrate ANSES into the circles of action (through its laboratories) or expertise (by mobilising its vigilance or assessment departments) in support of crisis managers.

Developing our contributions to risk governance means first of all consolidating the new 2022 missions (expanded role in socio-economic assessment, transfer of assessment tasks from the High Council for Biotechnology, finalisation of the transfer of missions resulting from the ASAP Act) and, under the new goals and performance contract (COP), preparing for the missions whose assignment to ANSES is being examined: vigilance and assessment missions relating to cosmetics and tattoo products, contribution to supporting the Indoor Environment Quality Observatory with the French Scientific and Technical Centre for Building (CSTB).

Developing our contributions also means setting up methods for cooperation in expert appraisals with other agencies and institutes, when it is necessary to go beyond ANSES's core competencies to answer increasingly global questions, in particular to take the impacts on biodiversity into account.

To better play its role in risk governance, ANSES must also review the way it interacts with stakeholders, in order to usefully assist them in the profound transitions that will take place. In line with this, the new Social Sciences, Economics & Society Department (DISSES) will conduct a debate on how dialogue is organised between ANSES and its stakeholders, in order to improve the existing mechanisms. The Agency will also strengthen its interactions to support other players in this dialogue, such as the French Economic, Social & Environmental Council (CESE), the National Consultative Ethics Committee (CCNE) and the National Commission for Public Debate (CNDP).

Changes are inevitable in the short and medium term, whether driven by the younger generations, who by nature have a different perspective, or the not so young, who are confronted with the realisation of numerous tensions. It is essential to use the contributions of ANSES's different activities to shed light on these changes, and this will largely be achieved by continuing the various exchange interfaces it has established and consolidated since its founding.

As an illustration, in 2016, the Agency pioneered the development of dietary guidelines, determined by taking account of physiological needs and the harm caused by different contaminants. It is clear that future food production systems will increasingly need to take their overall environmental impact into account, paving the way for other parameters to be factored in when establishing such guidelines. Furthermore, the global changes in production, processing, distribution and consumption patterns associated with environmental and climate phenomena could lead to the emergence of new hazards or the re-emergence of known ones. The Agency will be particularly vigilant on this, as the greater the changes, the harder it will be to safeguard health.

These general orientations have been broken down, as they are every year, into **orientations for each of ANSES's five areas of activity**: food safety and nutrition, animal health and welfare, environmental health, plant health, and occupational health. Although presented by area, their implementation often requires cross-cutting efforts between the teams carrying out the Agency's activities.

A number of orientations per area are based on the national plans in which ANSES has a leadership role or to which it contributes (PNSE4, SNPE2, PST4, PNNS, EcoAntibio, Ecophyto+, etc.).

Consistency in the implementation of these orientations is also down to the work of ANSES's cross-functional scientific departments in seven fields – food, epidemiology & surveillance, antimicrobial resistance, exposure to & toxicology of chemical contaminants, plant health, animal health & welfare, occupational health – which stimulate collaboration between the research, reference and surveillance activities, and help develop synergies between them and the Agency's spheres of action in scientific risk assessment and regulated products.

Breaking down these general orientations and organising them by area of activity, the summaries prepared by each operational division detail the projects for 2023, showing the main themes in sheets for each action. These include action sheets for the functional departments devoted to international action and communication.

The 2023 work programme shows that all ANSES's missions and activities specifically take account, in detail, of the issues to which it must and wishes to respond in a radically changed context, in order to consolidate its role as a reference player and proactive source of proposals for the public authorities and society. It thus reflects the Agency's ambition to:

- continue acquiring knowledge to support expert appraisals;
- contribute to the development of scientific methods and tools to better detect and assess risks, and enhance them with socio-economic assessment components;
- anticipate, identify and characterise health risks, including in times of crisis;
- develop an increasingly integrated approach to risk assessment in support of the One Health approach;
- prepare during 2023 the transfer to ANSES of new missions concerning cosmetics, tattoo products and the Indoor Environment Quality Observatory, subject to the decisions and goals of the new 2023–2027 COP.

Given the multiplicity of risk factors and the complexity of global mechanisms for understanding the whole One Health concept, ANSES is also convinced that tomorrow's health and safety system will be brought about by greater cooperation and deliberate complementarity between national and European agencies, and research viewed at an increasingly European and international level. It therefore continues working at these scales to consolidate all its reference and risk assessment activities and its work on regulated products, which has led it to step up its participation in major European research projects and partnerships under Horizon Europe, the European framework programme for research and innovation, which began on 1 January 2021 and will run for seven years.

With the growing need for insights into health issues, in 2023 ANSES will continue its efforts to make its scientific conclusions and recommendations accessible and share them widely with stakeholders, decision-makers and the general public, as well as to explain the approaches it has adopted in the area of ethics and collective adversarial expert appraisals, and to provide insights on its methodological principles, especially those relating to levels of evidence and taking uncertainties into account. In accordance with its mission to contribute to public debate, ANSES will continue to make its work fully available for the initiatives and discussions taking place in its areas of competence.

II. Strategic orientations

Food safety and nutrition

Animal health, welfare and nutrition

Environmental health

Plant health and protection

Occupational health

Food safety and nutrition

Background

Food safety and **nutritional issues** are major societal challenges due to their economic and health consequences; they are a central concern to many citizens, who have high expectations for healthier and more sustainable food. This perception was reinforced during the COVID-19 lockdown, with expectations in terms of food safety, and changes in access to food with greater use of short supply chains.

Implementation of the **French EGAlim Act**[1], which is designed to provide universal access to healthy, high-quality and sustainable food, takes on new resonance with the importance attached to **improving the quality and safety of our food**, at the highest level of the State.

Food must now be **"healthy, safe and sustainable"**; it must cover all these dimensions along the farm-to-fork supply chain, including environmental aspects. Other topics also need to be considered, such as **food waste** or the issue of **food contact materials**, especially plastic packaging.

Moreover, **new consumption trends are emerging** and the link between health and nutrition is being questioned from a societal perspective more than ever before. Food is seen as an essential social topic about which everyone is entitled to an opinion, because of the global health and environmental challenges it raises for the future.

All these topics are taken into account in the EU's Farm to Fork Strategy for a fair, healthy and environmentally-friendly food system, which sets out a number of specific actions covering the entire food supply chain. This strategy, announced by the European Commission in May 2020, is one of the components of the European Green Deal announced in December 2019.

ANSES is addressing these complex debates supported by the robust scientific capabilities in its research and reference laboratories, skills in risk assessment, and major surveys and observatories mobilising both the fundamental sciences and the human and social sciences. All these strengths help it provide the tools and knowledge needed to shape an objective and recognised source of information in a context where false and often dangerous statements flourish and spread, particularly via social media. In this context, ANSES strives to remain a reference scientific player in **assessing the health and nutritional risks and benefits of food**, by upholding the highest standards, a strong forward-looking and integrative capability, and an openness to dialogue, as well as active participation in European and international work.

Challenges

Strengthen control of health risks to ensure safe food

Health crises due to chemical or biological contaminants are still very topical, and are a sign that controlling food-related health risks, even those that are well known, remains a fundamental challenge for public authorities, consumers and society more broadly. The expected global changes in production, processing, distribution and consumption patterns associated with environmental and climate phenomena could lead to the emergence of new hazards or the re-emergence of known ones. Controlling these health threats in food products and water necessarily requires a risk assessment approach that relies on the knowledge provided by surveillance and reference activities focusing on health hazards, as well as by research projects carried out by our laboratories, among others, in order to meet the objectives presented in the work programme of the Research & Reference Division's laboratories.

In particular, it involves identifying and characterising emerging or new biological hazards by deploying novel analytical techniques using genomics, metagenomics and "-omics" approaches more broadly, and detecting markers of interest to public health associated with the virulence, antimicrobial resistance, toxicity or infectivity of these

[1] Act No. 2018-938 of 30 October 2018 on the balance of commercial relations in the agricultural and food sector and healthy, sustainable and accessible food for all (for more information: https://agriculture.gouv.fr/egalim-tout-savoir-sur-la-loi-agriculture-et-alimentation)

biological contaminants and host-pathogen relations, with a special focus on interactions with the microbiota. Identifying chemical contaminants from natural, anthropogenic or multiple sources will require innovation and the use of novel, high-resolution, multi-residue, non-targeted technologies to extend our knowledge of the exposome and of interactions between chemical and biological compounds, and study the associated cocktail effects.

Controlling and assessing health risks also relies on knowledge of overall exposure documented in total diet studies (TDSs) which, along with data from monitoring and control plans, are used to estimate dietary exposure to many chemicals found in food. The Third TDS will pay particular attention to organically produced foods and certain substances specific to diets with a large vegetarian component. Other studies will focus on specific risks, such as the ChlorExpo study on exposure of the French Caribbean population to chlordecone.

The structuring, quality and analysis of the data generated by the monitoring activities rely heavily on the Agency's Contamine system for data from the monitoring and control plans, and on the SCA platform for food-chain surveillance, which is coordinated by ANSES working closely with the DGAL and INRAE. This enables an integrative analysis involving all the relevant food chain players. Thus, the SCA platform offers a collaborative, multidisciplinary and open framework to provide methodological and operational support to its partners and promote more efficient monitoring. The increasing volume of analytical data generated requires the implementation of a strategy and infrastructure to enable their computerised storage, accessibility, interoperability and reprocessing. This will be the focus of a topic to be addressed in a more general framework.

Document the food supply, and the nutritional benefits and risks for a healthy diet

The increase in the incidence of diet-related non-communicable diseases (diabetes, cardiovascular diseases, some cancers) is a reminder of the crucial importance of nutritional issues in public health. The challenges associated with this area are as follows:

- Identify food composition and supply through the data of the French Food Observatory (OQALI) run jointly with INRAE, and the Ciqual database, one of the most comprehensive in Europe, which includes detailed data on the average nutritional composition of foods consumed in France.
- Collect the data needed for risk assessments in the area of food and nutrition, for biomonitoring and for monitoring the population's health status, by setting up a large continuous national survey to replace the previous INCA and Esteban studies, jointly with *Santé Publique France*.
- Document the influence of cultural behaviours and determinants, in particular the extent to which physical activity or the level of sedentary behaviour are in line with health guidelines. Burning issues concerning the rate and quantity of food intake and their influence on health parameters will be central to the topics to be discussed. In this context, contributions from the human and social sciences are often essential; expertise in social and economic sciences is expected to become increasingly important in ANSES's work.
- Assess the risks associated with inadequate nutritional intakes by developing statistical and computational tools for quantitative risk analysis based on data collected through the Individual and National Studies on Food Consumption (INCA studies).

Anticipate new risks and trends to ensure evolving and integrated assessments

The methodology for future risk assessments will require the development of knowledge on and greater consideration of aggregate exposure and exposure to mixtures of several substances (cumulative exposure). In this context, it will be necessary to carry out integrative work in which toxicological questions are added to purely nutritional ones, and including a debate on the role of the exposome in the development of chronic diseases or certain metabolic diseases. ANSES will in particular work on methodological and scientific developments, which will contribute to a better characterisation of exposure to health hazards and the use of tailored risk assessments. Implementation of the European Partnership for the Assessment of Risks from Chemicals (PARC) coordinated by ANSES is a great opportunity to address these complex issues by strengthening European collaboration and complementarity. The strategic research and innovation agenda will enable the establishment of collaborative research projects on surveillance, exposure, hazard characterisation or risk assessment, and the development of new scientific concepts and tools to address the challenges of chemical risk assessment.

These concepts of exposure are supplemented by emerging risk factors linked to new consumption habits and behaviours that influence diet. Particular attention will be paid to new products, technologies, recipes and consumption patterns. These include novel foods within the meaning of the legislation: foods resulting from genetically modified organisms (GMOs) will be studied at the same time, by developing risk assessment in addition to examining individual applicant dossiers; the same will be true of "nanos" used in foods, newly-formed substances and herbal food supplements, whose consumption is increasing sharply.

Anticipating new food risks also involves activating ANSES's various vigilance and emergence monitoring schemes, in particular nutrivigilance and toxicovigilance, as well as the knowledge provided by the expert working group on plants. The potential impacts of plant protection products in food are identified through the phytopharmacovigilance scheme. These schemes are supplemented by the collection of health signals and alerts coordinated by ANSES in its fields of competence.

There is a need for more integrative risk assessments that consider the overall impact of food practices, particularly in terms of sustainability, to ensure healthy, safe and sustainable food. This initiative should involve the relevant partners. This highly integrative work should address a number of societal issues, such as consumer expectations and behaviour, and the outlook for food in the face of climate change, health crises, etc. It should take account of nutritional issues with balanced diets, health aspects in terms of food safety and occupational or environmental exposure, issues of sustainable production and consumption methods, including home-grown food consumption, as well as ethical issues associated with animal welfare, special diets, etc.

Participate in national, European and international exchanges and cooperative projects to fuel collective expert appraisals

At the national level, there will be different forms of collaborative effort to consolidate the One Health approach promoted by ANSES. As an example, the national reference laboratories (NRLs) will continue their rapprochement and cooperation with the national reference centres (NRCs). These mainly focus on food- and water-borne zoonotic pathogens as part of surveillance and reference activities in investigations of human cases or health signals or alerts, and also as part of research projects that consolidate knowledge of targeted contaminants posing a public health hazard. Close interaction with the work carried out by *Santé Publique France* on various topics (foodborne illness outbreaks, PNNS, biomonitoring) ensures synchronisation of the two agencies' missions and avoids redundancy and possible blind spots. Lastly, the development of joint complementary research with the scientific community of other research organisations (INRAE, CIRAD, CEA, Ifremer, Inserm) will be encouraged under framework agreements or the implementation of joint calls for thesis projects.

At the European and international level, scientific exchanges of data, biological materials, risk assessment models and methodologies, and scientific personnel will continue to be encouraged, particularly with those of ANSES's peers with whom it has already forged partnerships, some of which have been formalised by agreements. This is the case in the European Union with the BfR and FLI (Germany), DTU-Food (Denmark), RIVM (Netherlands) and ISS (Italy), and internationally with the FDA (USA), Health Canada and CFIA (Canada), NIFDS (South Korea) and SFA (Singapore).

The already very active and close collaboration with EFSA will be maintained and reinforced with the support of EFSA's national focal point at ANSES, through projects or action plans seeking to improve the efficiency of the data collection systems already in place, such as the contribution to the drafting of the annual report on zoonoses in the European Union, or through new systems such as the genomic data collection project, part of the One Health Molecular Typing System, for which ANSES is coordinating the provision of French data in conjunction with the DGAL.

Following on from the pivotal research and cross-cutting projects supported by the One Health European Joint Programme (EJP) coordinated by ANSES, which will end in late 2023, new opportunities for significant European calls for projects will be sought, in order to continue the collaborations initiated under the One Health approach, particularly on the topics supported by the One Health EJP: foodborne zoonoses, antimicrobial resistance and emerging risks. In this context, ANSES will apply an active and dynamic approach to participating in the establishment of future partnerships under the Horizon Europe programme for research and innovation. This major seven-year programme is a great opportunity to strengthen partnerships and cooperation on a European scale, and is fully in line with the European Green Deal for a clean and circular sustainable European economy, to restore biodiversity and cut pollution. Alongside the European Partnership for the Assessment of Risks from Chemicals (PARC), which was launched in May 2022, other partnerships that contribute to the EU's Farm to Fork Strategy for a healthier and more sustainable EU food system, a cornerstone of the European Green Deal, are being set up and are of major strategic interest to ANSES. These include the partnership on Animal Health and Welfare, in which ANSES has a particularly strong leadership role within the European working group tasked with preparing it, the partnership on Antimicrobial Resistance, in line with the One Health approach, and the partnership on Sustainable Food Systems, for which ANSES is involved in the preparation and is taking particular care to ensure the inclusion of health, safety and risk/benefit assessment aspects.

Animal health, welfare and nutrition

Background

Animal health, nutrition and welfare are themes that mobilise several of ANSES's entities, whether in terms of research, reference, surveillance, monitoring or assessment of risks and regulated products. Within a multidisciplinary agency that covers veterinary public health, plant health and public health in relation to food, the environment and work, these animal themes are often at the intersection of One Health issues, bringing together humans, animals and the environment. This has been clearly illustrated by recent health crises such as COVID-19, brucellosis in the Haute-Savoie, swine influenza, avian influenza, etc. Because humans and animals may share the same ecosystems, because wild animals know no borders and because farm animals are increasingly kept outdoors in our country, the animal health, welfare and nutrition sector must now regularly question the interactions between these different compartments, increasingly anticipate the emergence or re-emergence of infectious diseases, consider new control strategies, study the spread of antimicrobial resistance, assess the risks to animals from environmental contaminants, and explore the interactions between different pathogens and contaminants.

While climate change and the measures adopted to mitigate it are a growing concern for public health, they also affect animals. This is true not only with regard to the new health hazards that may threaten them and humans, especially through arthropod vectors whose range is expanding in our part of the world, but also with regard to changes in the availability of food resources for animals, along with the use of new raw materials or additives, leading to the assessment of new products and even new potential risks.

These background points raise important issues for the Agency's activities that contribute to the establishment of ANSES's work programme in the area of animal health, nutrition and welfare; a programme that also takes into account a changing regulatory environment, with the European landscape currently being reshaped with regard to animal-related activities.

Challenges

Increasingly anticipate health crises through research, reference, monitoring, surveillance and risk assessment

The lessons learned from the two major avian influenza health crises in 2021 and 2022, the crisis of COVID-19 as a disease that can be shared with animals, the spread of African swine fever in Europe, and the alerts constituted by human cases of zoonotic swine influenza have all led to similar findings on the need to provide tools to better anticipate health crises. At ANSES's level, the Agency is focusing its animal health work programme in this direction, both in research and reference, to identify and develop **methods for ever earlier detection**, using new molecular approaches and diversifying the matrices that can be analysed, in order to detect pathogens **before the first clinical signs**, and with the aim of providing **on-site tests for sick livestock animals** that are feasible and effective.

Antimicrobial resistance projects are being pursued with the same objective, to **better predict the phenotypic resistance of bacteria** based on their genomes. Better anticipation of crises also requires **continuous improvement in the way infectious animal diseases are monitored**. ANSES's goal is to provide the various surveillance stakeholders with the scientific and technical support necessary for the effective management of epidemiological surveillance data. The work programme activities carried out within this framework include assessing and improving surveillance schemes, contributing to an integrative intersectoral approach (One Health aspect), health monitoring and methodological support.

Regarding **monitoring of antimicrobial resistance**, in 2023 the **Resapath** network will continue its participation in the national meta-network PROMISE, which links together all the professional networks addressing antimicrobial resistance in the human, animal and environment sectors.

Anticipation also requires the **development and continuation of research on health hazards likely to emerge or re-emerge**, identified as such by scientists thanks to their knowledge of animal pathogens. COVID-19 demonstrated that the immediate and engaged response of our laboratory teams to the pandemic was only possible because of the pre-existing expertise on animal coronaviruses within our scientific community. The emergence of canine brucellosis in France and, more broadly, in Europe, shows the importance of the work of the ANSES laboratories, which keep a constant **watch over regulated pathogens**. The laboratories' work programme therefore includes a non-negligible share of scientific activities on these health hazards, as well as non-targeted research. The laboratories' numerous **European and international reference mandates**, as well as ANSES's participation in international health monitoring, also help guide research in this spirit of anticipation.

Through collective expert appraisals, **risk assessment** also plays a major role in providing health authorities with scientific evidence, **ahead of and throughout health crises**. By mobilising the full range of scientific skills in a **multidisciplinary approach**, ANSES fulfils its mission to respond to formal requests from risk managers, both in anticipation, ahead of the preparation of action plans (swine influenza), and through emergency collective expert appraisals when required by current events (animal epidemics such as avian influenza or industrial accidents that could potentially contaminate animal feed). ANSES is also committed to **capitalising on all its past work** in order to provide rapid scientific and technical support based on its previous opinions.

Study, document and assess pathogen-animal-human-environment interactions

Several of ANSES's activities contribute to **improving knowledge of the interactions between pathogens, their hosts and their environment**. By using a variety of complementary approaches (ultrastructural, -omic, cellular, functional, etc.), the ANSES laboratories working on animal health aim to **better characterise the health hazards** affecting or threatening France, their expression according to their hosts and their persistence in different environments. With many pathogens, the challenge is to better characterise the **role of the environment in pathogen transmission** to domestic animals: persistence in soil, water and microfauna, fate of infectious agents in manure spread on land, or during burial, composting or anaerobic digestion processes, etc. **Answering these questions requires both research and risk assessment**.

Regarding the environment, the objectives are also to **explore the receptivity/susceptibility of wild animals to infectious agents** of interest and to determine the consequences of this susceptibility on wildlife populations, in order to identify **possible reservoirs** of infectious diseases in the environment. In order to identify the different factors favouring the spread and perpetuation of pathogens, on scales ranging from the animal up to the ecosystem, other scientific fields are also mobilised: **epidemiological research** to explore the interactions between the different compartments (the environment and human, animal and plant health), and **risk assessment** to provide insights that enable managers to make their decisions. Responses to several **formal requests** are on the risk assessment work programme for 2023, **involving all or some of the three pillars of the One Health concept: animals – humans – environment**. Among other things, they intend to make advances in knowledge of the role of foxes in the dynamics of certain infectious diseases, assess the risk of botulism in relation to wildlife, and produce risk maps for tick-borne encephalitis in France.

This same One Health approach is also applied to the field of antimicrobial resistance, for various studies on molecular characterisation of the resistome and **genetic carriers of antimicrobial resistance determinants in different environments**. These studies enable **assumptions to be put forward on the spread of antimicrobial resistance** and possibly on source attribution between animals within sectors, between sectors at national level and/or regarding cross-transmission with humans.

The animal environment also includes arthropod vectors. The importance of **vector-borne diseases** in the expected health consequences of global warming has been clearly demonstrated in numerous reports, leading ANSES laboratories to devote part of their work programme to **research on these infectious diseases, some of which are zoonotic**. This research involves the **characterisation of potentially emerging infectious agents** (such as Crimean-Congo fever virus), the study of **pathogen-vector interactions** (such as the exploration of the tick immune system) and the use of **epidemiology** and **risk assessment to characterise vector-animal and/or vector-human interfaces**.

Investigate and assess new control strategies

Advances in knowledge of infectious agents and their molecular interactions with the host on the one hand, and the lessons learned from recent health crises affecting or threatening France on the other, have generated respectively opportunities and needs to develop and assess new strategies to combat animal diseases.

The development and assessment of vaccine approaches to prevent health risks should be highlighted. Under the impetus of the French Presidency of the Council of the European Union in the first half of 2022, the principle of possibly vaccinating poultry against **avian influenza** was established. Experiments are under way at the **NRL** and will continue into 2023. The **French Agency for Veterinary Medicinal Products (ANMV)** will also be working on this topic. The **Risk Assessment Department** will be called upon to provide scientific evidence to support the determination of vaccination and surveillance scenarios for vaccinated flocks.

Regarding research and risk assessment, other work is planned on vaccination against various infectious animal diseases that threaten animal production sectors (such as African swine fever) and/or public health (such as *Salmonella* on poultry farms).
Lastly, innovative, more fundamental work is being carried out in this field of vaccination, both to develop **new routes of administration** (mucosal vaccination) and to define **new control strategies** (vaccination directed against the tick microbiota).

Besides vaccination, **other strategies** are being investigated, such as those using **antiviral substances** against various pathogens, with some of the projects having an element of animal → human **translational research**.

Better knowledge of the spread of animal diseases in order to adapt control measures is also an orientation included in the laboratories' research programmes. Improving knowledge of the spread of diseases in populations, and in ecosystems more widely, enables **future spread to be predicted and the impact of management actions to be measured**. The **epidemiological research activities** carried out within this framework use mathematical and statistical modelling, phylodynamic tools combined with whole genome sequencing activities, contact networks and the study of transmission chains.

The European timetable for assessing biocidal substances, which is currently focused on disinfectants, will lead ANSES to **assess the safety and effectiveness of substances used in veterinary hygiene**, such as quaternary ammoniums. This assessment work also helps improve the control of infectious diseases in livestock by targeting the relevant substances against the various pathogens. It also supports risk assessment: ANSES's assessment work on lime-based products was used for the expert appraisal on the burial of animal carcasses, conducted in 2021.
Another major theme of the control strategies work programme is **work on resistance to antiparasitics**. Resistance to antiparasitics has been investigated far less than resistance to antibiotics, which has become a major international public health issue. However, these resistance phenomena are currently harmful to animal health and can compromise certain production sectors. The challenge is to **provide alternative solutions to antiparasitic resistance** and, through discussions between different units within the Agency, to **explore the cross-cutting nature of resistance mechanisms**, from plants to animals and from bacteria or viruses to parasites.

Explore co-infection and co-exposure phenomena

ANSES is developing research projects to characterise the impact of co-infections or co-exposures in livestock animals, with a view to taking all animal exposure to health hazards into account in an integrated manner, as defined today by the **exposome** concept for humans. Several projects in the work programme will therefore focus on the **impact of pathogens co-infecting animals on the expression of infectious diseases of interest**, both for public health and animal health (mainly poultry and pigs). This approach can also be applied to other hosts such as vectors (particularly ticks).

In bees and fish, several projects aim to explore the **effects of animal co-exposure to infectious agents and chemical contaminants**, in particular by studying the impact on host immune systems.
These various studies are gradually contributing to the **emergence of the exposome principle** in the characterisation and assessment of health hazards **for animals as well**.

Animal welfare: an integrated approach to studying new livestock farming methods and continued research on relevant indicators of animal welfare in farming

The animal welfare research projects in the work programme focus on the **multi-criteria assessment** of new alternatives to conventional livestock farming methods, with an emphasis on an **integrated approach to animal health, public health, animal welfare and biosecurity**. The numerous examples of infectious animal diseases occurring in livestock farming highlight the difficulty of making approaches to controlling health hazards compatible in practice with approaches to take better account of animal welfare. Multi-criteria approaches are therefore needed to help reconcile the different objectives. ANSES will also continue its work on **animal welfare indicators**, which are essential tools for verifying the relevance of measures to **improve farm animal welfare, based on the animals' expectations and response**. The Agency's involvement in **reference activities in the field of animal welfare, at the French and European levels**, enables it to capitalise on its research in this field by translating it for animal production stakeholders (on farms, in transport or in slaughterhouses) and for the authorities tasked with regulatory control.

Lastly, **approaches combining animal ethology and the human and social sciences** suggest the potential for other exploratory fields in animal welfare, with the aim of adopting a **One Welfare** approach designed to develop a holistic view of human/animal welfare, taking account of potential interactions with the farm's socio-economic and ecological environments.

Adapting the Agency's work to a changed regulatory environment

Several major changes have been initiated in recent years at European and national regulatory levels. Implementation of the new regulations for France implies considerable work for the Agency that has been included in the 2023 work programme.

For the French Agency for Veterinary Medicinal Products (**ANMV**), efforts will continue on **implementing the new Regulation** (EU) 2019/6 on **veterinary medicinal products**: continuation of regulatory work to adopt secondary legislation at the EU level; continuation of work to adapt national law; implementation at the ANMV's level in its business processes.

The ANMV will also prepare for Cycle V of the Benchmarking of European Medicines Agencies. This project aims firstly to assess the management and operating methods of the veterinary medicinal product agencies in the Member States, with regard to the standard adopted for Cycle V of the benchmarking exercise, and secondly to draw on the other agencies' best practices identified during the previous cycles, in order to implement improvement opportunities.

For the **NRLs and EURLs** (national and European reference laboratories), 2023 will be partly devoted to adapting reference activities to the new regulatory context arising from implementation of the **Animal Health Law** (Regulation (EU) 2016/429 on transmissible animal diseases): new regulated animal diseases or new animal species covered, leading to an additional workload for the classic national and European analytical reference missions.

Implementation of the various measures to combat antimicrobial resistance at European level will also be accompanied by activities for ANSES, such as development (by the ANMV) of the **collection of data on the sale and use of antimicrobials** in connection with the Calypso project led by the DGAL. In addition, ANSES, which on the basis of its expertise in coordinating the Resapath network had been tasked with leading the European EARS-Vet initiative to **coordinate European surveillance of antimicrobial resistance in veterinary medicine**, will continue to pursue this ambition in 2023 and beyond.

In **animal nutrition**, the new Regulation (EU) 2020/354 establishing a list of intended uses of feed intended for **particular nutritional purposes**, provides for the possibility of adding new particular nutritional purposes to this list, after assessment of a dossier submitted by the applicant company. ANSES, which is responsible for assessing these applications, has included in its 2023 work programme the **drafting of guidelines for the assessment of application dossiers** on particular nutritional purposes, which do not currently exist.

In terms of French regulatory developments, the **ASAP** Act on accelerating and simplifying public action has repercussions on some of ANSES's assessment activities. It **transfers** to the Agency responsibility for issuing, amending and withdrawing **authorisations prior to the use for scientific research purposes** of substances not authorised by the European Union as **feed additives**. In this new context, ANSES issued an internal request to consolidate the guidelines on the content of the dossiers accompanying applications for authorisation to conduct trials.

With regard to **analytical reference** activities, the Agency's **NRLs and EURLs** will continue their involvement in the new CEN/TC 469 **technical committee for standardisation in animal health**, mainly in its working group on quality control of reagents.

The forthcoming publication of a ministerial order on classification of reagents with regard to the Animal Health Law will enable implementation of a **reagent control** system, with the **definition of a reference standard for batch-by-batch control**, on which ANSES will continue working in 2023.

Increasing ANSES's visibility through European and international undertakings

The Agency will continue working with its European partners to set up a future **European partnership on animal health and welfare** in the framework of **Horizon Europe**. If selected by the Commission and the Member States, this European partnership will seek to become the keystone of European research and reference in animal health and welfare for the next decade.

With a view to **harmonising surveillance of animal diseases at European level according to a One Health approach**, ANSES will be an **EFSA** stakeholder in the **One Health subgroup** of the EFSA Animal Health and Welfare (AHAW) Scientific Network. Its tasks will be to reflect on the prioritisation of animal diseases to be monitored, and to participate in designing the surveillance strategies to be applied.

Lastly, the work planned for 2023 by the various laboratories holding **European** (7 mandates in animal health and welfare) **and international reference mandates** (26 WOAH and FAO mandates in animal health) gives ANSES great international visibility and also provides a broad vision, beyond our borders, of animal health hazards.
Similarly, the ANMV will maintain its international positioning under its mandate as **WOAH Collaborating Centre for veterinary medicinal products** and the Agency will continue supporting the FAO within the framework of its mandate as **FAO Reference Centre for antimicrobial resistance**, for which it will mobilise all its expertise to contribute to the four themes developed by the FAO in its plan to combat global antimicrobial resistance.

Environmental health

Background

The One Health concept refers to the fact that there are close links between human health, animal health and ecological status. As an example, human health is impacted by environmental factors such as the quality of water, air or soil, or by noise and artificial lighting. This includes the consequences of unsustainable consumption patterns, demographic growth and its territorial distribution, and human activities, mainly those linked to industrialisation, urbanisation and the development of insufficiently controlled technologies. Climate change, which has a major influence on the environment, ecosystems and biodiversity, is the priority issue for the coming years in terms of assessing the associated risks.

Assessing environmental risks requires identifying situations and modes of exposure and vulnerability to the effects of the chemical, biological and/or physical agents concerned. The many uncertainties in this field regarding their interactions with living organisms and their combined or cumulative effects (whether simultaneously or over successive periods of life), which are covered by the concept of the exposome, pose a major challenge to knowledge. By demonstrating the various determinants of exposure, the levers for action able to control them can be identified.

In addition, expert appraisal work and support for research on risks that have generated strong scientific and social controversy should continue to feature prominently in the Agency's activities. These include health risks associated with endocrine disruptors, nanomaterials and pesticides, as well as risks potentially associated with rapidly developing technologies.

The environmental health actions to be developed over the next three years must learn from these findings and be consistent with the national plans that determine ANSES's priority expert appraisal and research needs, with European and international orientations (regulatory and research), the Agency's monitoring activity, and the optimised use of vigilance and research data.

The Agency's action in the field of environmental health will therefore focus on several themes:

1. **Anticipate emerging threats and risks** associated with changes to the environment and climate that are sources of scientific and societal controversy;
2. **Improve expert appraisal practices** to more effectively guide public decision-making, particularly by seeking to:
   - identify vulnerable populations and critical exposure situations, particularly foetal/embryonic development and the first few years of life;
   - identify collective and individual uses and behaviours, together with the socio-economic determinants that dictate the circumstances and modes of exposure, which are sources of social and environmental inequalities;
   - use methodological breakthroughs on assessing the weight of evidence and uncertainties in expert appraisal work;
   - optimise regulatory assessments by participating in the European "One substance, one assessment (OSOA)" initiative.
3. **Develop the risk assessment tools** (cost-benefit studies, socio-economic studies, etc.) needed to ensure that risk management recommendations are better taken into account;
4. **Develop interdisciplinary methodological tools** to enable assessment of the risks associated with mixtures as well as integrated risk assessment (exposome): cumulative risks, aggregate risks, human/animal/plant interfaces, use of biomonitoring and vigilance data, occupational and non-occupational exposure, taking exposure factors into account;
5. **Support research in environmental health and improve its synergies with expert appraisal**, particularly to obtain data that will provide insights on the exposome, and develop prospective studies on the risks of the future, especially through support for the National Research Programme for Environmental and Occupational Health (PNR EST) and its calls for proposals;
6. **Strengthen European and international collaboration** by participating in research consortia, reinforcing bilateral relations with our counterparts, and contributing to the work of European organisations such as EFSA, the EEA and ECHA, or international organisations such as the WHO, etc.

Challenges

Chemicals: a strong ambition that goes beyond the Chemicals Strategy for Sustainability (CSS)

The use of chemicals is regulated in the European single market to ensure a high level of protection for European citizens and their environment. Following the EU's adoption of the Chemicals Strategy for Sustainability (CSS), which represents the first step towards the "zero pollution" ambition for a toxic-free environment announced in the European Green Deal, revision of the REACH and CLP[2] Regulations is under way. The Agency is involved in preparatory work to improve health and environmental protection. It will continue its assessment of chemicals under the current regulations, as well as its analyses of the best risk management options (RMOA), its identification of substances of very high concern (SVHCs), its proposals for restrictions on use when risk situations are identified and, within the framework of the CLP Regulation, its classification proposals, including on the new hazard classes that are keenly awaited from the ongoing developments: the endocrine disruption hazard and new environmental hazard classes such as persistent, mobile and toxic (PMT) substances.

ANSES has been tasked with the scientific and administrative coordination of the European Partnership for the Assessment of Risks from Chemicals (PARC), which was launched in May 2022, and will also be making a significant scientific contribution to several of the programme's work themes. The goal of PARC is to provide chemical risk assessors and risk managers with new data, knowledge and methods, and to develop the network of specialist players and the scientific skills required to address current, emerging and new challenges in chemical safety. Three EU agencies (EFSA, EEA and ECHA) are involved in PARC, which broadens the partnership's scope, particularly in the process of identifying its priorities for action. ANSES will also continue to participate in the work of the WHO's Chemical Risk Assessment Network, whose objective is to improve chemical risk assessment by fostering interactions between organisations.

It will also include in its expert appraisal work the elements resulting from the new European action plan for the circular economy.

At the national level, the Agency is closely involved in the development of various health reference values (HRVs), such as toxicity reference values (TRVs), indoor air quality guidelines (IAQGs) and occupational exposure limits (OELs). These are essential tools for quantitative risk assessment and the definition, for example, of regulatory concentrations that should not be exceeded in order to protect health.

The Agency also provides scientific input to the authorities in the following specific areas:

- **Endocrine disruptors (EDs)**

ANSES is committed to the Second National Endocrine Disruptor Strategy (SNPE2). It is continuing to assess substances with ED potential according to the prioritisation methodology published in 2021 and a list of substances defined annually following input from several Thematic Steering Committees. The results are presented at European level (REACH and CLP Regulations, etc.). The Agency also assesses the ED properties of all active substances (plant protection products and biocides) for which it is the competent assessment authority.

- **Nanomaterials**

In a context of great uncertainty about the risks posed by nanomaterials to human health and the environment, the Agency's work in 2023 will aim to identify those that are both of little use and of significant risk. In connection with Action 13 of the PNSE4, this work will aim to describe the industrial sectors that use nanomaterials, based mainly on the use of data from the R-nano register that the Agency will continue to manage.

[2] Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures

- **Chemical mixtures and the exposome**

The Agency will be pursuing its activities, particularly through its work in PARC in conjunction with its European partners, to develop the methodological foundations for ranking the priority chemical mixtures to be considered in its health-related expert appraisals and in the preparation of HRVs for chemical mixtures. Following on from this, the Agency will also use the report drawn up by its Scientific Board to advance the methodological foundations for implementing the concept of the exposome in its work.

- **Biocides**

To date, only a minority of biocidal products have been granted marketing authorisation (MA). The challenge for the coming years is the full implementation of European Regulation (EU) No 528/2012 and the regulation of all biocidal products in Europe. This requires, first of all, ANSES's strong commitment to advancing the active substance review programme, and also to the assessment of MA applications for biocidal products, with a view to national or EU marketing authorisations. To this end, the Agency actively participates in the methodological developments carried out at European level, on issues that emerge as new product categories are assessed.

- **Consumer goods**

The lack of knowledge on the chemical composition of many products, the presence of undesirable contaminants in some of them and, more generally, questions on the safety of numerous products highlighted in previous risk assessments of exposure to **consumer products** have prompted the Agency to continue its efforts. In the new French legislative context resulting from the AGEC Act (against waste and for the circular economy), the Agency will focus its work on identifying new product uses resulting from recycling. In connection with the PNSE4, ANSES will be proposing a calculation method to assess the overall criticality of the health and environmental hazards associated with the use of household products, intended to clarify their labelling.

While the composition of **tobacco and vaping products** is now better known due to the reporting obligation introduced by the Tobacco Directive (2014/40/EU), assessment of the risks associated with their consumption is hampered by the complexity of the mixtures, the variability of the emissions formed and the partial documentation on the hazards associated with inhalation of the ingredients and additives they contain. The Agency will continue assessing the risks associated with vaping products that present an opportunity to quit smoking, and pursue its participation in the second European Joint Action on Tobacco Control (JATC 2), which offers an opportunity to work with the European partners most committed to this topic.

Focus on challenges related to water

The new Directive (EU) 2020/2184 on the quality of water intended for human consumption came into force on 12 January 2021 and the Agency was actively involved in providing scientific support to the Directorate General for Health in drawing up the texts that transpose it into French law.

Assessments of materials in contact with water will be affected by the future regulatory framework for the quality of drinking water to be implemented from January 2023, and the Agency is closely involved in work to harmonise assessments of materials compliance, led by the European Commission and ECHA.

The Agency provides scientific support to water management stakeholders by assessing the risks associated with the chemical contaminants – some of which are emerging substances – such as pesticides and their metabolites that may be found in drinking water, water resources and aquatic environments more generally.

The Agency is also involved in the area of recreational water, including the issue of health risks associated with *Ostreopsis* spp.

All these activities should be placed in the context of the impact of climate change on the various environmental media, a particularly sensitive subject with regard to water resources (availability, modification of its characteristics, etc.) and the reuse of non-conventional water sources (wastewater, black water, rainwater, etc.), on which the Agency provides support with regulation. The Agency is also proposing to focus on the potential consequences of climate change on water resources by identifying and ranking the associated health risks.

Focus on challenges related to air

ANSES will remain active on the topic of outdoor and indoor air pollution.

Among the main issues to be addressed by the Agency are those relating to mixtures of substances in the air, including ultrafine particulate matter, black carbon and pesticides, as part of the strengthening of EU legislation on ambient air quality.

Regarding indoor air, the issues at stake are the assessment of risks associated with all the vectors of exposure specific to indoor environments: chemical, biological and physical agents – including temperature – and multi-source exposure that comes under the concept of the exposome.

The foreseeable developments due to climate change concerning the presence of certain agents in the air justify an assessment of the medium-term health risks.

Physical agents: technological innovations and noise

The Agency will maintain its monitoring activities on the impacts of new technologies, whose uses are constantly evolving.

Expert appraisals to update knowledge on the possible links between radiofrequency exposure and the occurrence of cancer will continue, along with support for the Cosmos-France study run by the International Agency for Research on Cancer (IARC) to collect data on population exposure to electromagnetic waves and health.

In addition to the health effects of electromagnetic fields, the use of digital technologies can have other types of health effects, especially by modifying behaviour. In 2023, the Agency will continue the expert appraisals already initiated to assess these effects and their determinants on the physical and mental health of children and adolescents.

With regard to noise pollution, which has a considerable social cost in France, while its extra-auditory effects are increasingly well understood (sleep, cardiovascular, cognitive and school learning problems, etc.) this is not the case for the impacts. In order to prepare for a future assessment of the health impacts of noise pollution, the Agency will continue to monitor changes in sources and modes of exposure to noise. As part of the PNSE4 actions to reduce exposure to noise, and in a context of strong social and environmental inequalities, the Agency will initiate a debate on how to assess the health benefit that can be derived from the implementation of noise reduction/attenuation measures. In addition to ANSES's work on the impact of noise on human health, the effects of noise on biodiversity should be the subject of particular attention using a One Health approach.

The challenge of vector control

Given the spread of arthropod vectors of pathogens for humans, animals and plants through space and time, the Agency will actively pursue the actions initiated in the field of vector control (VC) and vectors, in particular assessing the risks of arbovirus outbreaks in France and their associated socio-economic impacts, and developing a methodology for prioritising the entomo-epidemiological investigations to be carried out around cases of arboviruses imported into metropolitan France.

Given the small number of authorised active substances of interest for VC on the market, particular attention will be paid to the effectiveness of alternative control methods (sterile insect technique, etc.) and vigilance with regard to resistance.

Most of this work is related to the implementation of French public policy actions (Lyme Plan, PNSE4, Bedbug Control Plan, Pandemic Plan, Climate Plan, etc.).

Plant health and protection

Background

France's agricultural, forestry, landscape and environmental plant health situation is affected more and more by the consequences of the increased frequency and volume of world trade in plant products, the impacts of global climate change, and changes in farming practices and crop management techniques.
At European level, a new Regulation (EU) 2016/2031 on protective measures against pests of plants, known as the "Plant Health Law", has been in force since the end of 2019. It identifies the organisms harmful to plant health whose entry and establishment must be prevented, and allows for a regular update of the corresponding lists according to advances in knowledge and data acquired. Greater worldwide awareness of the corresponding issues had led to 2020 being declared the International Year of Plant Health by the United Nations General Assembly (https://www.ippc.int/en/iyph/). More than ever, this context requires early identification of the emerging or re-emerging risks that may result.

In addition, growing concerns about the impact on health and the environment of treating crops, forests or non-agricultural areas with plant protection products (PPPs) are fostering greater use of biocontrol products and a reduction in the number and quantity of PPPs used. These changes, resulting largely from regulatory incentives, also make a significant contribution to the emergence of new problems associated with harmful organisms.

Some elements of this context may increase the risk of introducing new pathogens and pests into France, lead to the emergence or re-emergence of new plant health issues, or even result in "deadlocks" being identified where no effective treatments can be authorised. It should also be emphasised that France possesses considerable overseas territories, which are ecologically fragile and particularly exposed.

With the mobilisation of two of its laboratories (the Plant Health Laboratory – LSV and the Lyon Laboratory), the Risk Assessment Department (DER), the Regulated Products Assessment Department (DEPR) and the Market Authorisations Department (DAMM), the Agency adopts a comprehensive approach to plant health and protection by studying the interactions between plants, pathogens and pests, and the regulated products used, while considering all the health, economic and societal elements.

The Agency's mobilisation and active contribution are continuing in Europe and internationally, in all areas: risk assessment, authorisations, research, reference, monitoring, surveillance and vigilance. The Agency is pursuing its involvement in the work of European and international institutions (mainly EFSA, ECHA, EPPO and the IPPC), as well as with its counterparts and partners in Europe and more broadly internationally (Canada, United States, Maghreb countries, etc.), particularly given the importance of mutual information and alert in combating the risks that emerge and spread between countries or continents.

Challenges

Health risk assessment and national monitoring for better anticipation and prevention

Because the new European regulation emphasises prevention, and a growing number of plant health hazards are also impacting other living compartments as considered in the One Health approach, risk assessment – with its corollaries of prioritisation and anticipation – will mainly take place in areas where plant health and human health overlap. An example of this is exposure to processionary caterpillars with stinging hairs that defoliate woody forest species, with an analysis of the health risks associated with exposure to these caterpillars and the formulation of management recommendations. In addition to the usual aspects, this work will include an analysis of the joint risk to humans and biodiversity.

As current changes to the climate are significantly altering the areas and conditions of prohibited pests' potential establishment in France, it is also necessary to update these conditions, especially in the case of regular interceptions, as has been the case with the oriental fruit fly over the last two years.

Another consequence of the current regulations is to establish the conditions under which quarantine pests, plants or plant products may be introduced or circulate in the European Union. It therefore makes sense to assess the risks of environmental contamination, and to identify effluent treatment solutions for quarantine pests handled by laboratories.
Lastly, in line with the increased need for vigilance, ANSES's assessment mission will continue using an innovative approach to pre-empting emerging risks, through continuation of the EFSA-funded European programme Horizon Scanning for Plant Health.

Again according to a preventive approach, but this time relating to a national monitoring activity, ANSES will play an ever more central role in coordinating the national epidemiological surveillance platform for plant health run with the DGAL, INRAE, the FREDON network, Acta, the Chambers of Agriculture and the French Agricultural Research Centre for International Development (CIRAD), by jointly leading or participating in thematic working groups (tomato brown rugose fruit virus – ToBRFV, *Xylella fastidiosa*, the bacterium responsible for huanglongbing – HLB, Panama disease in banana crops) or project teams (oak wilt). Involvement in monitoring emerging resistance to PPPs will continue within the framework of the "Unintended effects and Resistance" component of the biological surveillance of France (SBT) being carried out by the DGAL, while at the same time benefiting from methodological innovations such as high-throughput sequencing and considering the gradual prioritisation of biocontrol products in monitoring.

Detect and diagnose high-risk monitored pests using standards, technologies and methodologies that guarantee innovation and quality

The number of crises or major health concerns currently affecting France has increased significantly (*Xylella fastidiosa*, pinewood nematode and HLB, along with ToBRFV, Panama disease in banana crops, lethal yellowing palm disease and the oriental fruit fly). While always striving for optimal dialogue between our laboratory reference and research activities, our methodological efforts on innovative techniques for detecting and identifying regulated and emerging pests will take form through a range of approaches that are being ramped up: barcoding and metabarcoding, multiplex and multipurpose PCR tests, digital PCR and high-throughput sequencing, with the detection of emerging resistance to PPPs and implementation of bioinformatics pipelines, including on insect vectors of pests.

For GMOs, it has become essential to address the identification of products derived from new breeding techniques (NBTs). In this regard, although innovative methods will play an increasingly important role, the quality and efficiency of diagnosis will still require considerable effort on the more conventional biological approaches in a context of increasing scarcity of skills that remain crucial in view of the corresponding issues.

Continual improvement in the assessment of plant inputs...

The challenges identified for the coming years in assessing plant inputs, both for synthetic PPPs and biocontrol products, lie in the production of knowledge and methods to ensure that a high level of protection for human health and the environment is maintained and that the solutions placed on the market are effective.

To achieve this, the scientists of the DEPR have worked hard to develop or improve assessment methodologies. This work is most often undertaken in partnership with other organisations or in the framework of national, European or international working groups.

In addition, the importation into France and release into the environment of any non-indigenous macro-organism beneficial to plants requires a risk analysis by the applicant, which must provide the information needed to support its application for authorisation prior to use. The LSV and the DEPR will continue interpreting these risk analyses. The LSV will also be in charge of examining applications for the importation into France of macro-organisms used in work carried out for scientific purposes in contained conditions without release into the environment.
The DEPR will remain active in examining applications for the importation into France of macro-organisms for use in non-contained conditions. In order to facilitate the submission of applications for the release into the environment of non-indigenous macro-organisms beneficial to plants, a methodological guide specifying the information to be provided in such applications was submitted for public consultation in 2022, after finalisation of its examination, and its publication is planned for early 2023.

...while facilitating the submission of applications, optimising their processing and allowing easier access to information for issuing MAs

The Market Authorisations Department (DAMM), while ensuring that authorisations are managed in a way that complies with the ever-changing national and EU regulatory requirements, will continue work to adapt its procedures to facilitate the various stages of managing a dossier from start to finish, and ensure consistency with the new approved requirements.

This facilitation will take place in a context where the new conditions for re-approving some active substances and not renewing approval for others will lead to a restriction of the authorisation scope, a tightening of the conditions for use of products, and measures to protect human and animal health and the environment.

In this area, the DAMM will continue its efforts to optimise and simplify the management of applications by pursuing work on the D-Phy project to digitise dossier documents, which has now been opened up to all companies. The action plan to improve the timeliness of MA decisions will remain topical, with prioritisation of biocontrol products and simplification of processes.
The DAMM will continue to publish information notes online to promote a better understanding of the requirements and procedures. In order to facilitate access to information, the MA bulletins will also be made available on the website.

The department will continue work on the comparative assessment of products containing substances that are candidates for substitution. In particular, work has been carried out on applications for products containing copper compounds, in the context of the forthcoming renewal of MAs.

Lastly, in connection with the inspection activities entrusted to ANSES, cooperation with State inspection services will still continue, in order to facilitate field controls and ensure adequate understanding of the regulatory provisions concerning the manufacture, distribution and use of PPPs.

More rational use of plant protection products through characterisation and monitoring of resistance and identification and measurement of all unintended effects: phytopharmacovigilance

In a context where there are calls for a continuous reduction in the number and diversity of authorised active substances, resistance becomes a key issue: each treatment must be as effective as possible and its use reasoned in order to curb the evolutionary response of the target organisms. With this in mind, ANSES develops methods and tools for detecting resistance through both biological and molecular approaches, such as high-throughput sequencing methods for more precise surveillance and monitoring. The work carried out in this surveillance mission may also benefit the phytopharmacovigilance scheme (PPV, see below) through the early identification of emerging individuals carrying resistance. The corresponding research work focuses on investigating the mechanisms involved in resistance phenomena, while studying the parameters that influence the growth of PPP resistance in agronomic evolutionary landscapes.

Created under the French Act on the future of agriculture, food and forests, the purpose of the phytopharmacovigilance scheme (PPV) is to collect data on adverse effects occurring in humans, plants and animals and, more generally, in all environments and their resistance following the use of PPPs. It enables the continual reporting of information to benefit risk assessment, the placing of PPPs on the market and the risk management missions performed by ANSES's supervisory ministries. The main source of information reporting is the network of partner schemes, supplemented by reports that can be sent directly to ANSES via a reporting portal on its website. The scientific and technical literature and the press are other sources of information. ANSES is consolidating the processes to identify these signals.

Lastly, ANSES can initiate ad hoc studies on the adverse effects of PPPs when the information is incomplete or to further examine a report on an adverse effect. These are designed to help answer specific questions, whose results can then be used quickly, for example to adapt the conditions of an MA or define cross-cutting management measures. The actions planned for 2023 will form part of a renewed PPV strategy to be defined by the Agency for the period 2023–2028, and will integrate the coordination actions of ANSES's health vigilance schemes.

Occupational health

These strategic orientations are set in the context of implementation of the Fourth Occupational Health Plan (PST4) for 2021–2025 and are in line with the EU's strategic framework for health and safety at work for the period 2021–2027. They develop the main themes of its 2023 work programme that the Agency wishes to highlight on the basis of the work programme sheets.

Ensure active monitoring and vigilance work in order to identify emerging occupational risks

The detection of emerging or re-emerging occupational health risks is one of the Agency's fundamental missions that relies on monitoring, research and vigilance work. Thus, while pursuing its routine work to produce data and knowledge in support of expert appraisal or to develop tools for detecting emerging cases of new occupational diseases, in 2023 the National Network for the Monitoring and Prevention of Occupational Diseases (RNV3P) will continue its discussions on optimising the scheme, and on developing and harmonising the occupational exposure thesaurus coordinated by ANSES as part of the PST4. ANSES also manages or leads other vigilance schemes, such as toxicovigilance, veterinary pharmacovigilance and phytopharmacovigilance, whose functions and collection methods differ but which are also used to identify emerging adverse effects or health problems related to work. The vigilance data they generate provide regular exposure data and reports of cases used to document or initiate risk assessments.

Mobilise multidisciplinary scientific expertise to support public policies and decision-making in France and Europe

The production of knowledge on hazards and exposure, as well as the assessment of health risks, are central to the Agency's activities and expertise, especially in the area of occupational health. Much of this work concerns chemicals and is also related to implementation of French public policy actions (PST4, PNSE4, SNPE2, etc.) or decisions taken within the framework of EU or national regulations on the assessment and management of chemical risks.

ANSES will therefore continue its work in response to formal requests from the ministries or as part of its permanent missions to ensure a high level of support for public decision-making, particularly in the framework of developing OELs/biological limit values (BLVs), identifying and classifying carcinogenic work and processes, and carrying out expert appraisals prior to the creation or amendment of occupational disease tables.

In 2023, ANSES will also continue to provide a high level of support with expert appraisals conducted for European regulations **(CLP, REACH, Plant protection products, Biocides, Veterinary medicinal products)**. Most of these regulations include a component on occupational exposure and risks. European work on exposure assessment and changes in technical standards due to advances in scientific knowledge will be monitored to ensure overall consistency and harmonisation of practices among the various regulations. This will be facilitated by the diversity of regulatory fields within the Agency's missions. Harmonisation will be further promoted in the context of the EU's "One substance, one assessment" (OSOA) initiative developed as part of the "zero pollution" ambition for a toxic-free environment announced in the European Green Deal. ANSES is closely involved in the work arising from this initiative. The aim is also to leverage the expertise produced within this framework via the PST4 actions for improving information, occupational risk prevention and health protection in the workplace.

As far as possible, the Agency will also endeavour to step up its efforts, in all the expert appraisal work mentioned, giving priority to ED, CMR and nanoparticle substances, in order to improve knowledge of hazards and exposure, especially at work.

The major challenge for the Agency will be to maintain efforts already under way to develop new knowledge and robust methodologies to take the combined effects of chemical mixtures into account. More broadly, the Agency will strengthen its ability to work in a multidisciplinary way and integrate its various fields of expertise in order to apply the concept of the exposome to its expert appraisals, by implementing the action plan resulting from the work carried out by its Scientific Board.

Investigate multiple exposure situations more closely and anticipate the risks associated with new forms of work organisation

In the area of occupational health, for the past few years, the Agency has had to conduct complex expert appraisals related to a specific profession or industry, or to the particular ways in which work is organised. In this approach, multiple exposure and the assessment of combined risks is a central and recurring issue. This was the subject of a major study to characterise multiple exposure situations as part of the PST3[3] . The digital transition is also gradually disrupting all aspects of work, from its organisation to its purpose, including the ways in which it is carried out and the conditions under which it is performed. While these emerging technologies or new forms of work organisation can be empowering when workers are involved in their implementation, they can also have potentially negative consequences on their health. It is more vital than ever to investigate the impact of these new work situations and new technologies on workers' health, through a cross-cutting approach that considers all the risks they generate, i.e. in a situation of multiple exposure, and puts into perspective the various lessons learned from the Agency's work on this topic. In 2023, several expert groups will be continuing or finalising their work, which focuses "in practice" on occupational settings involving multiple exposure.

Air pollution, particles, dust: informing stakeholders from the world of work and raising awareness about an issue at the interface between environmental and occupational health

The issue of air pollution, in particular the risks associated with **fibres, dust and particles**, is a topic to which ANSES is particularly committed and on which it has produced a great deal of work in recent years. In the coming years, therefore, the Agency will be encouraging real mobilisation, information and awareness-raising on this issue in the world of work, in connection with the actions planned on this topic in the PST4. These actions will draw on the knowledge produced during the Agency's current expert appraisals on this issue.

Sustain the major contribution of the human, social and economic sciences to expert appraisals on risks to workers

Assessing risks also requires the precise characterisation of exposure, i.e. **identifying and understanding its determinants**. Thus, an analysis of the actual work activity, closely tied to labour relations, economic imperatives, the organisation of production (subcontracting, etc.) depending on company size and the industry sector, the legal context and the representations of the hazards and risks by the various players concerned, is necessary for a relevant assessment of uses and exposure. Consequently, in addition to "expology" (exposure science), turning to disciplines from the human and social sciences – such as economics, ergonomics or sociology – is essential in many cases. An understanding and a detailed analysis of the behaviour of stakeholders – whether consumers, workers or companies – in the face of the applicable regulations, and the ability of public or private institutions to implement and enforce these regulations, are all necessary dimensions for understanding exposure situations and therefore identifying risk situations and possible means of preventing or reducing them.

These skills are now deployed as part of a dedicated expert appraisal body within the Agency – the Expert Committee on socio-economic analysis – which will be regularly called on in connection with the various expert appraisals in occupational health.

Contribute to the development and visibility of occupational health research in France and at European level

Research and knowledge generation are essential to identify risks and develop a good understanding of the effects of exposure and working conditions on workers' health and safety. This research and knowledge also provide input for the expert appraisals carried out by ANSES, as well as for the decisions of public authorities.

[3] https://travail-emploi.gouv.fr/IMG/pdf/pst3.pdf

Under the National Research Programme for Environmental and Occupational Health (PNR EST), the Agency will give prominence to actions to support and facilitate occupational health research, in order to develop the knowledge and skills needed for its risk assessment missions in the medium term. The research funded within this framework takes into account occupational exposure (and multiple exposure) to chemicals, particles, magnetic fields, noise, etc. and focuses on its health impacts (respiratory health, cancer, effects on reproduction, etc.). The PNR EST has also incorporated the concept of the exposome in its definition, in order to encourage proposals for research projects that take greater account of multiple or combined exposure. These objectives are also in line with those of the PST4, to which the Agency will make a major contribution, mainly regarding actions devoted to research.

ANSES's teams are also involved in the preparation and implementation of research projects within the framework of European funding on subjects of major importance for the Agency. First and foremost of these is the European Partnership for the Assessment of Risks from Chemicals (PARC), coordinated by ANSES and launched in May 2022, and which will include many subjects related to occupational health. PARC aims to develop new tools (surveys, participatory science, data analysis, etc.) to gather information on the conditions of exposure at work (occupational scenarios) that influence overall exposure. This work will be used to make recommendations to reduce the most significant forms of exposure in terms of occupational health impacts.

Strengthen European and international partnerships

ANSES has continued to strengthen scientific exchanges with partners having similar functions, with whom it has established regular and close relationships. Some of these have been formalised by partnership agreements, whether in Europe with BAuA in Germany, and RIVM, GR and TNO in the Netherlands[4], in the United States with NIOSH, or in Quebec, Canada with INSPQ and IRSST[5]. These organisations are often consulted for contributions to expert appraisals, particularly on work already undertaken or ongoing in the various countries. Relations with European agencies (ECHA and EU-OSHA[6]) and international bodies such as the World Health Organisation (WHO), particularly its Chemical Risk Assessment Network, or the International Agency for Research on Cancer (IARC), should be continued.

[4] Federal Institute for Occupational Safety and Health (BAuA); National Institute for Public Health and the Environment (RIVM), Health Council of the Netherlands (GR), Netherlands Organisation for Applied Scientific Research (TNO)
[5] National Institute for Occupational Safety and Health (NIOSH), National Public Health Institute of Quebec (INSPQ), Robert-Sauvé Occupational Health and Safety Research Institute (IRSST)
[6] European Chemicals Agency (ECHA), European Agency for Safety and Health at Work (EU-OSHA)

III. Summaries of the work programmes of the Scientific Divisions

Research & Reference Division

Regulated Products Division

Science for Expertise Division

Research & Reference Division

Introduction

ANSES's Research and Reference Division brings together nine of the Agency's laboratories, along with the Strategy & Programmes Department (DSP), which is responsible for guiding the definition of the laboratories' scientific strategy and contributing to its implementation through the coordination of cross-cutting activities.

The ANSES laboratories carry out **analytical reference** missions (66 national mandates, 13 European mandates and 29 international mandates were held by these laboratories in September 2022) and **research** activities, and **contribute to surveillance** in the areas of animal health and welfare, plant health and food safety. In 2021, they also took on new missions relating to wastewater and sewage sludge monitoring. The laboratories also contribute to the **expert appraisals** carried out by the Agency in all these areas.

The **laboratories' work programme** is drafted and proposed in the form of detailed work sheets covering all the reference, research, monitoring and expert appraisal activities of the Agency's laboratories. These are then discussed with the supervisory ministries. They provide an overview of the path adopted by the various units, and can be used by managers for guidance, planning and dialogue with the supervisory ministries. These sheets, which are now prepared once every two years, have therefore been presented to the supervisory ministries for the period 2023–2024. Their mid-term update will be presented in autumn 2023.

The purpose of this note is to highlight, in addition to the cross-cutting projects led or coordinated by the DSP, the **main orientations and highlights for 2023 contained in these sheets, organised mainly according to the six cross-cutting strategic themes** defined by the Agency (animal health and welfare; plant health; food safety; antimicrobial resistance; epidemiology and surveillance; and finally exposure to and toxicity of chemical contaminants). These six themes, each promoted by a scientific director, help ensure coordination between the various entities, the efficient internal running of the Agency and the search for synergies between the laboratories' scientific units and with the risk assessment units, within their spheres of competence.

1. Cross-cutting projects led by the Strategy & Programmes Department

The DSP is responsible for supervising construction of the scientific strategy of the Agency's laboratories for research, reference and surveillance in conjunction with the departments in charge of risk assessment and regulated products. It is also responsible for contributing to the implementation of this strategy through the coordination and management of cross-functional activities, with the support of the scientific directors. In particular, it initiates, supports and leads actions that contribute firstly to harmonising, promoting and disseminating methods, products, resources and data from the laboratories, and secondly to ensuring the efficiency of schemes and compliance with ethical standards while carrying out the work.

Efficiency

The process led by the DSP to **harmonise and consolidate the reference activities of the Agency's laboratories, with a view to improving their efficiency**, will continue in 2023, mainly through the activities of an in-house working group tasked with proposing guidelines and tools for the convergence of **diagnostic reagent verification practices**, with a focus in 2023 on batch control by the NRLs. Next year will also see the in-house working group set up in late 2022 begin work on harmonising practices for **calculating and using measurement uncertainty**. A **reference panel** will again be organised in the coming year to keep up the momentum of exchanging practices and experience between French laboratories responsible for reference activities at national (NRL) and European (EURL/EURC) levels, along with an **in-house seminar for inter-laboratory proficiency test (ILPT) coordinators**, to continue promoting sharing and the search for common solutions in work in this area.

In the field of **biosafety**, inter-laboratory coordination efforts will be boosted in order to promote exchanges of experience, harmonisation of practices and development of shared tools to benefit all the laboratories. In addition, the DSP will continue the work undertaken with a view to making proposals to decision-makers on specific changes to the regulations on **micro-organisms and toxins (MOTs)** and the adjustments needed for their implementation, in order to minimise the difficulties and constraints currently encountered in research and reference activities. In this respect, recent emerging and re-emerging health threats (monkeypox, polio) have acutely illustrated the fact that our ability to respond promptly and effectively with work on these pathogens is still very much dependent on the provisions of the MOT regulatory framework.

Lastly, in 2023, the DSP, together with the Health Alerts & Vigilance Department (DAVS), will be coordinating preparation of the Agency's different entities (in particular the laboratories) for their mobilisation in the expected support for the health authorities' supervision of the **Paris 2024 Olympic Games**.

Major sector-specific projects

The coming year will see our teams mobilised to analyse the results of the **collective audit of ANSES's research and reference activity**, which took place in 2022, based on the recommendations made by ANSES's Scientific Board at the end of this audit. In particular, the following actions should be emphasised:

- formalisation of ANSES's scientific priorities for 2023–2027 to guide its research and reference activities;
- coordination and support for the laboratories in drafting their laboratory and unit orientation letters for 2023–2027;
- continuation of work to consolidate our policy on **biological assets**, in particular by finalising deployment in all laboratories of the IT solution for managing these assets, and by clarifying and disseminating our policy on external promotion in this area;
- continuation, with the help of the relevant support and cross-functional departments and in consultation with the Agency's other core divisions, of the discussions and work aimed at structuring the policy and implementation conditions for **managing and exploiting laboratory data**.

Scientific coordination for each of the six cross-cutting strategic themes (animal health & welfare, plant health, food safety, antimicrobial resistance, epidemiology & surveillance, exposure & toxicity of chemical contaminants) promoted by the six scientific directors will continue in 2023. This is intended to strengthen coordination and the search for synergies between the laboratories' scientific units and with the risk assessment units, by using incentives identified for each theme (seminars, funding of doctoral students under co-supervision, etc.). In 2023, particular emphasis will be placed on proposals for inter-theme coordination, based on the recommendations of the collective assessment, in terms of strengthening integrative coordination, including between the fields of microbiology and chemistry, and around the exposome and One Health concepts.

In order to facilitate this, the DSP will maintain its mechanisms for **allocating specific budgetary funding to teams for projects addressing major strategic challenges**. The projects selected in early 2022 under the third "cross-functional" call for expressions of interest, which seeks to break down barriers and bring together the Agency's different teams on subjects that are most often exploratory or proof of concept, will therefore continue and be completed in 2023. In addition, the projects proposed under the "flash" call issued in autumn 2022, selected by the DSP with regard to their fit with the strategic research and reference priorities (including in terms of collaborative strength with key external partners with whom the Agency has signed framework agreements, responses to questions from risk assessors, potential for industrial application, mobilisation of participatory research, etc.), will be carried out in 2023.

In 2023, the DSP will again administer a new **call for projects for doctoral grants** to encourage the hosting and supervision of doctoral students and maintain the circulation of new ideas within the teams. This will be a joint effort with INRAE, CIRAD, VetAgro Sup, the CEA and now ONIRIS and Ifremer.

Lastly, in 2023, the DSP will again organise **ANSES's Scientific and Doctoral Days** (JSDA) dedicated to the work of all the Agency's scientists. As well as promoting the scientific excellence of the Agency's entities – especially its laboratories – on topics of importance to ANSES, the objective is to foster synergies and exchanges of information between the Agency's scientists on its research, reference, surveillance, risk assessment and regulated products activities, while marking an important step in the training of the doctoral students hosted at the Agency.

Changes to address the challenges

Work will continue in 2023 to promote the **deployment of new technological approaches in the laboratories**, in particular the use of whole genome sequencing (WGS) or high-resolution mass spectrometry (HR-MS), in the reference and surveillance activities. This will enable the Agency to carry out its diagnosis and surveillance activities faster, more efficiently and with increased robustness, in order to safeguard public health.

In 2023, the DSP will also continue to implement **ANSES's policy of industrial application and partner relations with private players**, adopted and published in 2020, to share and make available to private teams the research results, biological resources and data generated by the Agency's laboratories, within a clear contractual framework tailored to serve public health. The objective is to further the necessary development of health tools, while complying with ANSES's obligations of independence from private interests. In this respect, the DSP will continue its efforts to seek partnerships with the SATT technology transfer accelerators, modelled on the agreement signed in September 2022 with the SATT Ouest Valorisation, in order to be able to rely as much as possible on these trusted third parties in the industrial application processes.

Scientific and institutional cooperation

The DSP will continue to support the laboratories in **developing scientific and institutional partnerships** in an ever-changing context. It will oversee effective implementation of the framework partnership agreements signed with various research and technical organisations (INRA, CIRAD, Ifremer, ACTA, etc.) and propose new structural partnerships if needed. In particular, it will continue to develop partnerships with players in the human public health sector (*Santé Publique France*, ANRS-MIE, Aviesan Alliance, the MIE and PREZODE calls for priority research programmes and equipment (PEPR), as part of the France 2030 plan, etc.), including by capitalising on the relationships forged or strengthened since 2020 as part of the response provided to the COVID-19 pandemic crisis, according to the One Health approach. In addition, efforts to structure links with environmental health players, particularly the French Biodiversity Agency (OFB), will be pursued.
The DSP, and in particular the six scientific directors, will support the laboratories as needed to move forward with **regional partnerships**, relying on our positioning in the various COMUE university groupings and our laboratories' standing with the Regional Councils.

The process of **strengthening cooperation between NRLs and national reference centres (NRCs)** will be pursued in conjunction with *Santé Publique France*, with the aim of further strengthening mutual knowledge and understanding, which is the basis for further cooperation, particularly in terms of contributing to the epidemiological surveillance of zoonoses and non-zoonotic agents that are pathogenic to humans.

Lastly, the DSP will continue its joint management of the three epidemiological surveillance platforms, along with its partners.

Europe and international

As in previous years, the DSP, working closely with the European & International Affairs Department (DAEI), will be devoting significant efforts in 2023 to the forging of **European partnerships for Horizon Europe**[7]. These will markedly shape the European research landscape in our fields of activity.

[7] European Union Framework Programme for Research and Innovation for the period 2021–2027

The DSP, together with the DAEI, will be heavily involved in overall coordination and implementation of the scientific and cross-cutting activities of the **European Partnership for the Assessment of Risks from Chemicals (PARC)**, launched in May 2022 for a seven-year period. Bringing together nearly 200 partners from 28 countries and three European Union agencies, and with an estimated budget of over €400M, the goal of PARC is to develop the next generation of chemical risk assessment to better protect health and the environment.

Besides its work on coordinating and implementing PARC, the DSP, together with the DAEI, will pursue its central involvement in preparing the partnership on animal health and welfare, and will continue to closely monitor the establishment of other partnerships of interest (especially those relating to food systems, antimicrobial resistance and pandemic preparedness).

After nearly six years, the **One Health European Joint Programme (EJP)** will come to an end in September 2023. This partnership project, which is being funded by the European Commission and the project partners, brings together 44 European human and animal health and food safety institutes from 22 countries. It is being coordinated by ANSES and focuses on research in the areas of foodborne zoonoses, emerging risks and antimicrobial resistance. The DSP will continue to be closely involved in representing the Agency in the consortium, within the Scientific Steering Board, and coordinating our laboratories' mobilisation for the scientific activities undertaken within the EJP, in collaboration with the DAEI, which is coordinating the project in partnership with its Belgian counterpart Sciensanso.

In 2023, the DSP will continue to represent the Agency, with the DAEI, and possibly coordinate the laboratories' mobilisation in various European or international initiatives (for example, the direct grant of the EU4Health programme on surveillance systems under the One Health approach for cross-border pathogens that threaten the EU, in conjunction with EFSA, if it is ultimately decided that France should apply).

In addition, the DSP will continue to **manage the European Union Reference Centre (EURC) for the welfare of poultry and other small farmed animals**, a reference centre that mobilises the dedicated scientific and technical resources of the Ploufragan-Plouzané-Niort Laboratory and several European partners.

ANSES laboratories may also be called on to contribute to international cooperation work with priority countries and partners for France and Europe, often in conjunction with the Ministry of Agriculture's international cooperation players (France Vétérinaire International and France AgriMer), for instance as part of EU twinning projects or bilateral agreements, or initiatives carried out under WOAH, FAO or WHO reference mandates.

2. Laboratory activities for the animal health and welfare theme

Animal health and welfare is an area of excellence for the Agency's laboratories and represents the essential potential of French reference and research in this field. These activities at ANSES combine high-level scientific skills and technical equipment, animal models that can be compared with alternative models, field experience in breeding different animal species, and multidisciplinary expertise interfacing with the Agency's other entities responsible for risk assessment and veterinary medicinal products, as well as at the European and international level.

This combination of skills and resources allows the Agency to be particularly responsive in supporting its supervisory ministries in the control of animal and zoonotic diseases and, where necessary, management of health crises. t enables ANSES to apply a comprehensive and systemic approach to issues of research and assessment in animal health and welfare, taking account of farming systems and their consequences on animals, on the health of professionals involved in animal production and on the safety of foods of animal origin, but also their possible interactions with wildlife, while not overlooking the specific health risk posed by resistance to antibiotics and antiparasitics in veterinary medicine. It therefore provides the State with the science-based evidence that is essential for establishing and supporting the implementation of risk management measures in all these areas. Lastly, its approach to research questions relating to "animal welfare for animal health" is an original one that is able to meet society's expectations in terms of quality, safety and ethics in animal production.

The scope of ANSES's missions covers many areas of human, animal, plant and environmental health. It includes recent health events such as COVID-19, swine influenza, and monkeypox infection, which have questioned the links between several of these compartments, placing the Agency at the heart of One Health issues. For the animal health and welfare theme, this approach now needs to evolve towards a more general concept of "One Health – One Welfare", which the Agency intends to continue integrating into its work programme in the years to come. The laboratories' work programme is also in line with this concept, whenever the issues of these different fields converge.

The ANSES laboratories' 2023 work programme in the field of animal health and welfare intends to meet the scientific challenges of research, reference, monitoring, risk assessment and support for risk managers in the following areas:

- **developing methods for detecting animal diseases** for analytical reference activities, in order to develop different diagnostic approaches enabling greater precision (sequencing, molecular characterisation) on the one hand, and greater speed on the other, for the earliest possible diagnosis, which could go as far as assisting professionals in dispelling doubts on the farm;
- **understanding the pathogenesis of zoonotic, regulated and emerging infectious animal diseases** or those with a major economic impact on the production sectors, by exploring host-pathogen relationships, from the organism down to the cell or even the cell ultrastructure;
- **epidemiology of these diseases and the various animal epidemics** they cause in France, by combining field investigation approaches with cutting-edge technologies in sequencing and molecular epidemiology, modelling and the detailed study of transmission mechanisms;
- **studying the mechanisms behind the crossing of the species barrier**;
- the **effect of co-infection and co-exposure on** pathogen expression;
- research into **new control strategies** for animal diseases, particularly through **vaccine approaches**;
- **improving animal welfare** for the benefit of animal health.

Some examples of the planned 2023 implementation of these major strategic themes are highlighted here.

Adapting reference activities to the new context of the Animal Health Law

In 2023, the ANSES laboratories with national and European reference mandates will have to **adapt their activities to the new regulatory context**. This concerns new regulated animal diseases (Surra, porcine reproductive and respiratory syndrome) and new animal species covered (small ruminants/camelids and llamas for the EURL for brucellosis, glanders and melioidosis, for example), and will lead to new reference materials, the organisation of new inter-laboratory tests and the adaptation of diagnostic methods; development of certain reference mandates to include support for professionals on health programmes of collective interest, etc. This adaptation will result in an additional workload for the classic national and European analytical reference missions.

In addition, as always, the national reference laboratories will **support the authorities in the event of any health crises** occurring in France. It should be noted that 2022 was marked by several crises, in particular the major avian influenza epidemic, the emergence of *Aethina tumida* in bees on Reunion Island, and the re-emergence of brucellosis in Haute Savoie in connection with an outbreak in ibex.

Animal disease detection methods: monitoring, innovation and adaptation to health crises

- The development of increasingly powerful tools for characterising pathogens and their genomes has opened up numerous opportunities for research, **innovation** and method development to **speed up the diagnosis of infections, facilitate early detection of highly contagious diseases and identify pathogens more precisely**. For instance, the Agency's **sequencing platforms** are continuing to adapt to growing demand for pathogen identification using whole genome sequencing, and different tools and technologies will be deployed in the laboratories such as **MinION** sequencing (e.g. for infectious fish diseases and bluetongue), **digital PCR** (DIGIDIAG project spanning the ANSES laboratories), **aptamer-**based technology (*Trichinella* spp, *Cryptosporidium* spp, *Giardia duodenalis*, *Anaplasma phagocytophilum*), etc. **Serology techniques** will also need to evolve (e.g. study of the test based on the P22 protein complex for diagnosing **tuberculosis** in particular species such as the badger). These new techniques facilitate and/or reinforce the diagnosis and precise identification of an infection's immunological signature, as illustrated by the work being pursued on **antibody repertoires** in pigs (porcine respiratory complex, pestivirus), which will then be developed for rainbow trout and chickens.

- The increasingly systematic **sequencing** by the reference laboratories of infectious agents they receive not only enables more precise identification but also, thanks to advanced analysis of the sequencing products, provides **decisive support in the epidemiology of infectious diseases**, the phylodynamics of pathogens and the identification of transmission chains during infection episodes (e.g. avian influenza, tuberculosis, brucellosis, etc.).

- **Innovation** also means continually adding **new matrices to which the analysis methods must be adapted**. Whether it concerns improving early detection of an infection, including by adapting to samples taken from the farm environment (highly pathogenic avian influenza), or studying transmission of pathogens (e.g. botulism, tuberculosis, brucellosis, tick-borne encephalitis virus, echinococcosis, lyssavirus, etc.) more generally by also exploring environmental matrices (dust, water, soil, bat guano, etc.), as well as various animal products, or analysing the effect of certain organic matter treatment techniques (composting, anaerobic digestion) on the persistence of infectious agents (e.g. agents of Q fever and paratuberculosis), **work on adapting methods to multiple matrices will be a challenge for the next work programme**.

- The reference laboratories will also be committed to **helping reorganise diagnostic and outbreak reporting schemes** for the infections most likely to lead to animal epidemics, in order to confirm/refute suspicions more quickly, where possible. **Transfers of partial confirmation methods** will be organised, mainly for avian influenza, paying particular attention to the traceability of samples and data along the chain to the NRLs, in order to maintain the centralisation of information, strains and sequences, with a view to continuing scientific activities and, in particular, establishing the phylodynamic analyses needed for understanding transmission chains, in support of management decisions.

- Lastly, the **numerous European and international reference mandates** held by the ANSES laboratories gives them a very broad view of infectious animal diseases and provides them with valuable data for **international monitoring** of these diseases. This is the case, for example, with surveillance of foot-and-mouth disease, bluetongue serotypes, melioidosis, emerging *Brucella* species (such as canine brucellosis in Europe), Q fever, bee diseases, Aujeszky's disease, rabies, etc., for which the laboratories have expertise that is recognised at the European and international level.

Host-pathogen relationships: exploring the sub-cellular level to better understand infectious phenomena

Research on understanding the pathogenesis of animal diseases and the immune response of animals will continue in the laboratories, using a variety of complementary approaches (ultrastructural, -omic, cellular, functional, etc.), **in order to investigate the relationships between the host (vertebrate and/or invertebrate vector) and the pathogen (bacterium or virus)**.

The projects concern both regulated livestock diseases and other infections which, although not regulated, have a major economic impact on the sectors involved.

This research provides knowledge that **helps the authorities and professionals take steps forward in the detection and characterisation of infectious diseases** affecting or threatening France. It also enables **better targeting of control measures and leads to new strategies** for disease control.

- The **interactions between host and infectious agent proteins** are central to several ongoing and future laboratory projects. These include the finalisation of hIPsTER on tick-borne encephalitis virus, PersIstOmics and PersIFA on foot-and-mouth disease, IPPA on high-throughput mapping of host-virus interactions in African swine fever (ASF), and LAGMED for rabbit viral haemorrhagic disease.
- Projects are also being developed to study **interactions between the RNA of pathogens and the cellular proteins of their hosts**. This is the case, within the framework of the Laboratory of excellence in integrative biology of infectious diseases (Labex IBEID), with studies on flaviviruses (West Nile), the ExoTrich project to characterise the RNAs of exosomes produced by *Trichinella*, and work on genomic RNAs of pig viruses. The latter study is investigating the recombination mechanisms responsible for the emergence of highly pathogenic strains or recombinants that allow immune escape in viruses responsible for porcine reproductive and respiratory syndrome (PRRS) or pig coronaviruses (such as porcine epidemic diarrhoea).
- These molecular approaches are also deployed to better characterise the **interactions between virus-vectors and hosts**. For example, they can be used to explore in greater detail the role of the tick immune system in the persistence and transmission of viruses, as planned in the SIROCCO project on Crimean-Congo fever.
- Lastly, some original projects are now focusing on the interactions between pathogens and the "host + its microbiota" entity, also known as the "**holobiont**", in order to determine the impact of these microbiota on the host's response to the infectious agent. This is the case, for example, with the HOLOBASS project, which will study the effects of a viral disease on the **European sea bass** holobiont.

These different approaches (ultrastructural, -omic, cellular, etc.) are now seen as essential tools, implemented to **provide answers** to fundamental questions on the pathogenesis of micro-organisms: **cycles, transmission routes and mechanisms** (e.g. Usutu, tick-borne encephalitis virus, airborne pathogens); **host adaptation** (e.g. swine influenza virus, chlamydia); **virulence markers** (e.g. West Nile); **recombination effects** (e.g. PRRS); **co-infections** in hosts (porcine respiratory complex) or in vectors (ticks, parasite viruses); **crossing of the species barrier** (coronaviruses, avian influenza, swine influenza).

Better understanding of pathogen-animal-environment interactions

Understanding infectious phenomena in animals also requires investigation of the environment in which they are reared and the role potentially played by certain environmental compartments in the perpetuation, development and/or transmission of pathogens. Several infectious animal diseases have a strong environmental component. The **role of the environment in the transmission of pathogens to domestic animals** will therefore be explored for the study of several infectious animal diseases such as **brucellosis**, **chlamydia**, **melioidosis** and **tuberculosis**. Several of these projects are concerned with the study of **interactions between infectious agents and environmental amoebae**. This is the case with ANSES's BACTAMIBE cross-cutting project, which aims to develop a tool for the simultaneous detection of targeted bacterial agents and amoebae present in environmental samples. Another project in the 2023 work programme will investigate the role of environmental amoebae in the perpetuation and transmission of bovine tuberculosis and paratuberculosis agents.

The previously mentioned studies on the **adaptation of analytical methods to complex environmental matrices** also make a major contribution to the exploration of these pathogen-animal-environment links, whether for echinococcosis, botulism or Q fever, for example.

Lastly, the ecosystems in which farmed animals live include other wild species with which they may interact, directly or indirectly. The study of pathogen-animal-environment interactions also involves **exploring the receptivity/susceptibility of wild animals to infectious agents of interest, in order to identify possible environmental reservoirs of infectious diseases.** Examples include projects on wildlife relating to tuberculosis, Q fever or botulism, studies on the presence of *Baylisascaris procyonis*, a zoonotic nematode found in raccoons (the main definitive host and an invasive alien mammal in Europe), and work to map the risk of tick-borne encephalitis virus (TBEV) in France.

New control strategies

Advances in knowledge of infectious agents and their molecular interactions with the host (vector or definitive host) on the one hand, and the lessons learned from recent health crises affecting or threatening France on the other, generate both opportunities and needs for the development of new strategies to combat animal diseases.

- Many of the projects in the laboratories' work programme are geared to this objective, starting with research on **vaccination**: the current trials on vaccinating **ducks against avian influenza** will continue during 2023 at least. Work on the ASFV-989 candidate vaccine **against ASF** will also continue: following the study of its adaptation to multiplication in cell lines, the strain will be characterised at the genetic and biological levels (safety, vaccine effectiveness, risk of reversion). Vaccination studies will also be carried out on livestock diseases such as **PRRS**, where the safety of live attenuated vaccines will be assessed with respect to the risk of reversion or recombination; and on **autogenous vaccines** for control of ***Streptococcus suis***. Research on **new vaccine strategies** will take place, in particular the **SPIDVAC** project (2022–2025), under a Horizon Europe call for proposals, which will give ANSES the opportunity to apply the best approaches to define new vaccines for **foot-and-mouth disease** and **African horse sickness**. Research is also being carried out to identify **new strategies to enhance vaccine immunity in newborn animals**. **For public health purposes**, work to identify and characterise proteins of vaccine interest will seek to improve **vaccines against trichinellosis in pigs**. **Mucosal vaccination** is also a key project in the research programme, with a focus on **coronaviruses**. The aim is to develop a DNA vaccine platform targeting the digestive and respiratory mucosa of pigs to control porcine coronaviruses.

  Original research on vectors is also included in these scientific advances, proposing an approach using **vaccines directed against the microbiota of ticks** and other vectors, to control vectors and vector-borne pathogens.

  Lastly, together with the French Biodiversity Agency (OFB), ANSES will be contributing to the implementation and management of a project to **vaccinate badgers against bovine tuberculosis** in Dordogne.

- In addition to vaccination, **other antiviral strategies** are being investigated. Several projects in the work programme focus on research and assessment of **antiviral substances** against various pathogens, such as Gumboro disease virus in poultry, or viral infections of the human and equine central nervous system (flaviviruses such as tick-borne encephalitis virus, West Nile disease and alphaviruses, responsible for equine encephalitis). As part of the "Translational Antiviral Strategies" Chair of Excellence and based on work on antiviral compounds active against equine viral arteritis, translational studies will be carried out in the field of nidoviruses, among human viruses of the coronavirus family: SARS-CoV-1, SARS-CoV-2, SARS, etc.

- Another major thematic area of the work programme on control strategies is the **work on resistance to pesticides and the search for alternatives**. In particular, the **GISOVAL** project will be developed and set up to prove the benefits and feasibility of implementing **integrated management of strongylosis** by introducing complementary methods combined with the rational use of anthelmintics **in suckler sheep herds**, and providing tools and references for the effective deployment of this management. Also worth mentioning is a cross-cutting ANSES project, **GamAPI**, which is studying the mechanisms of sexual reproduction of two major **coccidia** (*Toxoplasma gondii* and *Eimeria acervulina*), in order to identify new therapeutic and/or prophylactic targets. Lastly, the recent creation of the **SABOT joint technology unit**, which brings together ANSES's PhEED Unit and the French Horse and Riding Institute (IFCE), is facilitating studies on the **resistance of certain horse nematodes to antiparasitic treatments** through close collaboration with horse owners and breeders.

Animal welfare: studying new livestock farming methods through an integrated approach to animal health, public health, animal welfare and biosecurity

- The animal welfare research projects in the work programme focus on the **multi-criteria assessment of new alternatives to conventional livestock farming methods**, with an emphasis on an integrated approach. For example, the **PIGAL** project: "Alternative **pig farming**: opportunities and risks associated with animal health, welfare and biosecurity" will begin its last year in operation.

  In **poultry**, the **COCORICO** project is taking a similar approach, in order to propose more sustainable farming systems that improve animal welfare and health while reducing the use of antibiotics. The same is true with the **Pecking Control** project, which will develop and implement an integrated approach to control frustration levels in laying hens to prevent pecking "outbreaks", while also using **digital tools** for precision rearing.

  Projects will also be developed on animal welfare and health in the context of **rearing young goat kids with their mothers**.

- Work on **animal welfare indicators in livestock farming** will also continue, with finalisation of the **CMOUBIENE** project to develop an operational tool for assessing and managing sheep and goat welfare on farms.

- As the European Union Reference Centre (**EURC**) for the welfare of poultry and other small farmed animals, ANSES will continue its work on indicators for assessing the welfare of poultry and rabbits on the farm, during transport and at the slaughterhouse, and work will be carried out on identifying poultry depopulation methods. In terms of reference activities, ANSES also contributes its expertise to the work of the National Reference Centre for animal welfare.

- Lastly, the Agency will continue its participation in the work of the **"One Welfare" joint technology network**, which intends to build a network for multidisciplinary exchanges between biotechnical sciences and the human and social sciences. It aims to jointly promote human and animal welfare by acting on the human-animal relationship and the design of livestock farming systems, and to develop a holistic view of human/animal welfare in livestock farming by taking account of potential interactions with the "environment", i.e. by considering the socio-economic and ecological environments of the farm.

Animal models and alternatives

ANSES maintains and uses a set of **animal models** that enable it to link mechanistic studies at the cellular or molecular level with the reality of the response of complex animal organisms. Not only can these animal models provide an appropriate response to questions on the pathogenesis of infectious diseases or the effectiveness of control measures, but they are also used to **validate certain alternative models** developed by the teams within the ANSES laboratories. This is the case, for example, with the development and validation of new 3D infection models (**equine brain organoids** for the study of flaviviruses and alphaviruses), as well as ***in vitro* studies for assessing control methods** (screening of antiviral substances, assessment of innovative control methods against *Cryptosporidium parvum* and *Giardia duodenalis,* using *in vitro* and *in vivo* models, etc.).

Animal health and welfare at the centre of many cross-cutting research projects at ANSES

Many of the projects in the ANSES laboratories' 2023 work programme have cross-cutting themes.

For example, animal health and welfare are naturally addressed in several projects on **antimicrobial resistance** (e.g. mycoplasmas and antimicrobial resistance), **food safety** (e.g. hepatitis E), and the **surveillance and epidemiology of infectious diseases** (e.g. predictive or evaluative modelling of ASF and highly pathogenic avian influenza (HPAI), molecular epidemiology and surveillance of HPAI, the OMAA observatory for honey bee mortality and weakening, the surveillance network for causes of equine mortality (RESUMEQ), understanding of the epidemiology of Q fever in French Guiana, etc.)

Other cross-cutting themes under development in this work programme include studies on **co-exposure of animals to infectious agents and chemical contaminants**. **Two families of animal species are pioneers in this field: bees and fish**. Projects are focusing, for example, on the identification of biological response signatures (metabolomics and/or proteomics) following exposure to pesticides or honeybee pathogens, in order to better understand the cause of the observed mortality through the detection of specific biomarkers. In fish immuno-ecotoxicology, studies will focus on the impact of endocrine disruptors on the thyroid and immune systems and the microbiota of different tissues. **Cross-cutting links between the biological sciences and human and social sciences** should also be mentioned, among the cross-cutting themes of this work programme. Citizen science is contributing to a project to better understand and assess the risk of tick bites in urban and suburban environments (private gardens) or during recreational activities in forests (orienteering). Socio-economic components will be integrated into work on modelling the spread of infectious diseases such as avian influenza or African swine fever. As part of the ExpAirCox project on Q fever, anthropological surveys will be conducted to determine stakeholders' perceptions of health risks. A "serious game" will be created with a view to the "peacetime" joint development of health policies for the prevention and management of Q fever.

Pivotal European partnerships

The Agency will continue working with its European partners to set up the future European partnership on animal health and welfare, which will be co-funded under the Horizon Europe programme. If selected by the EC and the Member States, this European partnership will seek to become the keystone of European research and reference in animal health and welfare for the next decade.

3. Laboratory activities for the plant health theme

The increased frequency, volume and diversity of world trade in plant products, the impacts of global climate change, changes in farming practices and crop management techniques and the consequences of growing concerns about plant protection products (PPPs) are now identified by all the parties concerned – production sectors, risk assessors and managers, consumers and citizens – as key factors in the changing plant health context. The resulting emergence of new issues associated with plant pests and the related means of control and management, whether in metropolitan France or in the overseas territories, must be considered while attempting to balance approaches related to risk prevention, sustainability of plant protection practices, environmental protection and food sovereignty.

Our reference, research, surveillance support and expert appraisal work for plant health and protection involves the following entities:

- the **Plant Health Laboratory (LSV)**, whose units all conduct thematic, technical and cross-functional work on biological risks to plant health – including from invasive plants – in cultivated, forest and natural environments. The LSV's scope also covers insects that are beneficial to plant health, detection and identification of genetically modified plants, and quarantine of plants introduced under import regulation waivers;
- the **Lyon Laboratory**, which studies resistance to PPPs through its Contracted Unit for Characterisation and Monitoring of Phenomena of Pesticide Resistance Development (CASPER USC) in partnership with INRAE's Plant and Environmental Health (SPE) Department, and assists with epidemiology and national surveillance through its Epidemiology and Surveillance Support (EAS) Unit.

The ANSES laboratories' work programme proposes a comprehensive approach to plant health and protection, which:

- involves studying interactions of pests with plants and their environment;
- mobilises expertise while interfacing with the Agency's other entities responsible for assessing biological risks to plant health and PPPs;
- considers the Agency's activities in the health, economic and societal contexts;
- contributes to training through research, by hosting and supervising doctoral students. The theses under way mainly focus on the use of new tools for the detection and characterisation of pests, the study of their genetic diversity, epidemiology and vectors, the study of the mechanisms of emergence of resistance to PPPs and their genetic basis, or the effectiveness of control strategies.

From the European Union to the French overseas territories: a renewed regulatory framework currently being finalised

Implementation of the **European Plant Health Regulation (EU) 2016/2031** relies on a new classification for plant pests, with Commission Delegated Regulation (EU) 2019/1702 listing priority quarantine pests for the EU that will be subject to a specific annual surveillance plan set up by each Member State, and Commission Implementing Regulation (EU) 2019/2072 listing other regulated species. Emerging pests are subject to emergency measures at European level on a case-by-case basis. In addition, France retains the option of taking action on its territory against certain pests that are no longer listed among the quarantine and regulated pests. On the other hand, as the French overseas *départements* and regions (DROM) are now considered as third countries, specific corresponding regulations will be put in place for the period covered by this work programme. As one of the most salient aspects of the new European regulations is their evolving nature, our analytical capabilities must also evolve, in particular by integrating more generic methodological and technological innovations or, conversely, those capable of discriminating below the species level. All these changes modify the scope of most of our national reference mandates and require skills to be reinforced on the pests that remain targeted by these mandates, as well as methodological developments that will be useful for their early detection and epidemiological surveillance. This will mainly be achieved through a reorientation of our study topics.

Related to this new European regulation, Commission Delegated Regulation (EU) 2019/829 on protective measures against pests of plants for scientific or educational purposes or varietal selection has also entered into force, and affects the framework of both our activities in confined spaces and our assessment of applications for approval from the various players.

Lastly, **Regulation (EU) 2017/625 on official controls** has led the European Commission to set up five mandates for the European Union Reference Laboratory (EURL) in plant health, whose activities started in 2019. Our three EURL mandates (plant-parasitic nematodes, insects and mites, fungi and oomycetes) will be included in the third work programme, with the main objectives, besides the organisation of ILPTs and training courses for the NRLs on the detection of regulated pests, being methodological development work to respond to regulatory changes.

From the regulatory framework to health crises in the field: increasingly numerous major health issues

Following on from the 2022 work programme, three pests will continue to receive particular attention in 2023 in the current French plant health landscape: the ***Xylella fastidiosa*** bacterium, the bacterium responsible for citrus greening disease also known as huanglongbing (**HLB**), and the **pinewood nematode**. ANSES will therefore continue to develop existing methods into more efficient molecular techniques on *Xylella fastidiosa,* whether on plants or on its insect vectors. From a research point of view, the study of its genetic diversity will continue, as will the study of vectors other than *Philaenus spumarius*. Lastly, we will continue to participate in maintaining the interface for consulting and visualising French surveillance data, and analysing these data (reports and maps). With the bacterium responsible for HLB, the recent publication of a real-time PCR detection method and the recent defence of a thesis on disease modelling in an island context (Reunion Island) will enable in-depth work to be carried out while ensuring that the network of official laboratories is consolidated with regard to the method transferred in 2022. Lastly, coordination of networks of official laboratories and participation in inter-laboratory tests for detecting the pinewood nematode on wood and in its insect vector will not only remain very active at national level, but will continue to take on a more European dimension as part of the EURL mandate.

At the same time, we will be increasingly focused on four other pests that have also become a major concern in France: tomato brown rugose fruit virus (**ToBRFV**), the phytoplasma responsible for **lethal yellowing palm disease**, the fungus *Fusarium oxysporum* f.sp. *cubense* tropical race 4 (**Foc TR4**) responsible for Panama disease in banana crops, and the oriental fruit fly ***Bactrocera dorsalis***. The new EU regulatory framework allows for a more effective response to new emerging threats through the publication of European decisions, and because ToBRFV is now included in the European regulatory framework and the official method has been drawn up, the inter-laboratory tests will be supplemented by the transmission and analysis of French data (see *X. fastidiosa*). With lethal yellowing palm disease, for which a new outbreak has been identified in Guadeloupe, we aim to validate an official PCR detection method. Regarding Foc TR4, in addition to supporting surveillance through our confirmatory analyses of the first positive cases and coordination of the network of official laboratories, we will remain involved in the definition of surveillance protocols. Lastly, because of the recurrent interceptions in France, primary importance will continue to be attached to the *Bactrocera dorsalis* species complex, whether as part of EURL activities or within the framework of a thesis that will be defended in late 2023, enabling us to respond to the needs of the DGAL regarding tracing the origin of individuals captured in France, mainly through the validation of high-throughput molecular tools for its monitoring.

For all the pests that make up this ever-larger health landscape, we will also continue to promote our methods at the European and international level to EFSA, the European and Mediterranean Organisation for Plant Protection (EPPO), the International Plant Protection Convention (IPPC) and other EURLs.

Standards, technologies and methodologies that guarantee innovation and quality

With the requirements of the new European regulations on accreditation and the need for more effective methods, our involvement in the reference mission will be characterised by implementation of ISO/IEC standards: 17025 for analyses and 17043 for inter-laboratory tests.

For our research mission, while always striving for optimal dialogue with our reference counterparts, our methodological efforts will focus on innovative techniques for detecting and identifying the above-mentioned regulated and emerging pests: barcoding and metabarcoding, multiplex and multi-purpose PCR tests, digital PCR through a cross-cutting collaborative project involving the Agency's laboratories, high-throughput sequencing techniques (Illumina, MinIon) encompassing the detection of emerging resistance to PPPs, and implementation of bioinformatics pipelines, including on insect vectors of pests. Technological innovation using high-throughput sequencing will also help improve post-entry plant quarantine to meet new regulatory requirements, and detect herbicide resistance in invasive plants. An innovation based on MALDI-TOF mass spectrometry via another cross-cutting collaborative project will aim to characterise nematodes.

For GMOs, the characterisation of techniques for detecting and identifying polymorphisms at the nucleotide level will continue, to enable identification of products from new breeding techniques (NBTs), and we will maintain our excellence in validating the detection of new events or improving extraction methods, having joined the European Network of GMO Laboratories (ENGL). Bioinformatics will play an increasingly important part in the laboratory's activities, although it is important to underline that morpho-biometric methods for identifying nematodes and insects and biological tests of PPP resistance – particularly relating to insecticide-resistant insects – will continue to require considerable effort in a context of increasing scarcity of skills that remain crucial in view of the corresponding issues.

Lastly, as part of the Horizon Scanning for Plant Health project with EFSA, an innovative methodology for monitoring the media and scientific literature will remain in use for the early identification of new emerging or re-emerging pests within the EU, consistent with the expectations of the new regulations and with a view to renewing the corresponding collaborative project for four years if the application is successful.

Structured partnerships that reflect our growing recognition within the scientific and technical community

Not only will 2023 see the continuation or launch of national and international collaborative projects (with EFSA on *Phyllosticta citricarpa*, ANR and Horizon 2020 Structure on phytoviruses, ANR on botany, CASDAR on phytoplasmas and nematodes, LabEx ARBRE on airborne forest pathogenic fungi, Ecophyto on vineyard weeds), but the structural and visible links with our academic partners will be expanded. This will be the case with the partnership formed via the Pesticide Resistance Forum and Research **(R4P) network** with scientists from four INRAE laboratories (Provence-Alpes-Côte d'Azur, Nouvelle-Aquitaine Bordeaux, Bourgogne Franche-Comté and Versailles-Grignon) and an expert from the DGAL, and via the **CASPER USC** (with INRAE's SPE Department). This will also be the case with the **NemAlliance cluster** (with INRAE's Brittany-Normandy Centre) for the study of plant-parasitic nematodes, the **Mycology contracted unit** (with INRAE's Ecology & Biodiversity Department) for the study of fungi and oomycetes that are pathogenic to forest species, and the **DIAGEPITROP partnership** for our unit based on Reunion Island (with CIRAD) on emerging pathogen and pest populations for the French overseas territories and the South-West Indian Ocean/Southern Africa/East Africa region. In addition, together with INRAE, we will begin setting up **associate partner laboratory status** for our Entomology and Invasive Plant Unit on the Montpellier site **with the Centre for Biology and Management of Populations (CBGP) joint research unit**.

One Health approaches will be fostered, especially as part of internal partnerships. As for the R4P network and more specifically for the CASPER USC, implementation of the ANSES-INRAE phenotyping platform should lead to a multi-species cross-cutting research project in 2023.

ANSES will continue to play an active role in coordinating the **national epidemiological surveillance platform for plant health**, which is being run with the DGAL, INRAE, the FREDON network, Acta, the Chambers of Agriculture and CIRAD, and will be jointly leading or participating in thematic working groups (we will begin co-leading the "*Xylella fastidiosa* surveillance" working group with the DGAL and INRAE, we will co-lead the HLB working group and participate in the Foc TR4 and ToBRFV working groups) or project teams (on *Bretziella fagacearum*), in addition to groups focusing on surveillance schemes for regulated or emerging pests and on methodological work relating to international health monitoring, health reports, data quality, etc.

In addition, by making our data available to the platform as needed, and through our close involvement in cross-cutting support (epidemiology, biostatistics, IT) and scientific support in analytical fields, our contribution to surveillance will become further entrenched. The Agency will also be involved in monitoring emerging resistance to PPPs within the framework of the "Unintended effects and Resistance" component of the biological surveillance of France (SBT) being carried out by the DGAL, while at the same time benefiting from the planned process to unify the classification of PPPs and considering the possible deployment of high-throughput sequencing. It is important to stress that 2023–2024 will be a period of transition, with the planned reshaping and reorganisation of the SBT through an adaptation of the resistance surveillance plan, which will gradually prioritise surveillance of biocontrol PPPs over that of conventional PPPs.

4. Laboratory activities for the food safety theme

Food safety is a major and historical area for the Agency, and interacts strongly with four other cross-functional themes (animal health, antimicrobial resistance, exposure-toxicology, epidemiology-surveillance). The laboratory activities carried out under this theme cover all the main food production sectors, from farm to fork, in addition to drinking water. They are largely in line with national and European reference mandates and contribute to surveillance programmes for chemical and biological contaminants potentially found in food and water, and affecting consumer health and public health more generally. Research in food safety is carried out to meet the increasingly complex and integrative expectations for healthy, safe and sustainable food. This work generates original data and new knowledge for risk assessment and provides scientific input for public decision-making.

Major health challenges identified and anticipated throughout the food chain

The Agency's laboratories involved in food safety conduct reference and surveillance activities, with complementary research as part of a continuum to contribute to expert appraisals through scientific and technical support on a vast number of chemical, biological and microbiological contaminants potentially responsible for short-, medium- or long-term adverse effects, infection or food poisoning in humans. Their work on chemical contaminants, whether of natural or human origin, is detailed later in this document through the "Exposure to and toxicology of chemical contaminants" theme and will not generally be mentioned in this section, despite it being integral to food safety.

The exercise of **reference mandates is an essential and major mission** in food safety, placing the laboratories at the heart of the reference system supporting the French and European competent authorities with regard to the obligations of Regulation (EC) 2017/625. The Agency has national reference mandates for foodborne microbiological contaminants (*Salmonella* sp., *Listeria monocytogenes (Lm)*, enterotoxin-producing staphylococci, *Campylobacter* sp., *Vibrio* sp. in fishery products, micro-organisms in drinking water, viruses in foodstuffs of animal origin excluding shellfish, foodborne parasites, *Echinococcus* spp. and contamination of fresh produce such as salads, strawberries and berries) and biological contaminants (histamine, marine biotoxins), and EU reference mandates for *Listeria monocytogenes* and coagulase-positive staphylococci. This structuring provides it with an **effective analytical arsenal geared to** all the contaminants covered by the reference mandates, and enables it to supply and transfer the newly developed and validated methods to all the approved laboratories responsible for first-line analyses. In addition, **the Central Veterinary Laboratory (LCSV)** is a part of the Agency and covers the official first-line analyses for several French *départements* (75, 91, 92, 93 and 94) under an agreement with the authorities (DGAL and Paris Police Prefecture). Like all the laboratories, the LCSV may be mobilised under reinforced surveillance plans and health alerts in connection with two upcoming international events to be held in France: the Rugby World Cup in 2023 and the Olympic Games in 2024.

Collecting or supporting the **collection of surveillance data** associated with microbiological and biological contaminants is a major challenge for assessing their changes through space and time. This approach is mainly based on the identification and in-depth characterisation of micro-organisms for the detection of emerging or re-emerging circulating clones, particularly virulent strains or strains belonging to a particular cluster. During 2023, therefore, the laboratories will be able to implement complementary analytical methods as part of monitoring and control plans or official controls for *Listeria*, *Salmonella*, *Campylobacter,* enterotoxin-producing *Staphylococcus aureus*, pathogenic *Vibrio* in live bivalve molluscs, parasites in fishery products, histamine and biogenic amines, and marine biotoxins. Some analyses will also be conducted under the Marine Strategy Framework Directive (MSFD), the Third Total Diet Study (TDS3), the Biotox-Eaux network, the surveillance networks led by the Agency (*Salmonella* network, *Listeria* network under construction), or other schemes such as the EMERGTOX plan for monitoring the emergence of paralytic marine biotoxins in shellfish.

All ANSES laboratories working on the food safety theme contribute in their respective areas of activity to the microbiological investigation of clustered episodes of human cases, outbreaks of foodborne diseases and food- or water-borne infectious diseases in conjunction with the competent authorities responsible for coordinating investigations, and the NRCs. In addition, although there is currently no reference mandate, strains of the *Bacillus cereus* group isolated during collective food poisoning episodes will be systematically characterised and any *Bacillus thuringiensis* potentially present in these episodes will be identified.

The surveillance platform for the food chain (SCA), whose coordination was delegated to ANSES in 2022 jointly with the DGAL and INRAE, provides support and drives the development of food safety monitoring, for the structuring and management of integrated databases, in a spirit of unity among all food-chain players. All the data collected, in particular on identification and characterisation of contaminants in the various food production sectors, will support **work related to risk assessment**, refine work on **source attribution**, and contribute to the **investigation of microbiological contamination from farm to fork**. The monitoring data will also be used to conduct studies and assess preventive and control measures for this contamination in the various production sectors, in particular for *Salmonella* and *Campylobacter* (Bter and SAPOKIT projects).

The research carried out by the Agency's laboratories in food safety generally aims to i) gain a better **understanding of the behaviour and circulation of pathogenic micro-organisms and their toxins** throughout the food chain and in other related environmental ecosystems (LILIS thesis, DECLIM project, projects developed with the Fastypers joint technology unit, OE-VTEC thesis on *E. coli* in aquatic environments, Toxmodel project on marine cyanotoxins, PaperFish project on the distribution of zoonotic parasites in fish), ii) extend knowledge on **the mechanisms of adaptation to various environments** during processing (VIBRATO project on the viability of bacteria subjected to stress, TBEV cross-cutting project to improve understanding of the risk associated with the tick-borne encephalitis virus and its persistence in raw milk and raw milk cheeses from goats and cows), iii) identify **the factors involved in virulence, toxigenicity, resistance and persistence**, whether in the animal sectors or the production environment (STEC MEAT project on pathogenic *E.coli* in meat, BIOCLIM project on *Lm* and *Salmonella* in the dairy and pork sectors, PERSISTANCE project for *Lm* in aquaculture, ANR ClostAbat project for characterising potentially emerging bacterial hazards such as *C. difficile* or re-emerging ones such as *C. perfringens* in the cattle, pork and poultry sectors, ANR BaDAss project on the virulence of bacteria of the *B. cereus* group). New, more integrative approaches are being developed, such as interactions between pathogens, and also **host-pathogen interactions**, in particular with the gastrointestinal microbiota in animals (RIMICIA project, Metavics cross-cutting project on the microbiota and metabolome of chickens, CONTALIM project). In addition, work has been initiated to improve understanding of the **interactions between chemical and microbiological contaminants** or other biological and environmental parameters (MICROVIR project with ecotoxicological aspects, SUBLIM project on *Lm* for surfaces in production plants) in order to better define and characterise the nature and complexity of **exposomes**. This work provides data for **risk assessment** (Btimpact project financed by EcoPhyto2 to measure the health impact of bioinsecticides based on *B. thuringiensis*, INFESTANI cross-cutting project to analyse metadata on fish infestation by Anisakidae) and for defining **innovative approaches for the control** of these pathogens (REZOLVE, NewProb's and Sanimetha projects).

Technological and methodological innovations for the detection of emerging hazards

The recent review of the organisation of whole genome sequencing (WGS) at the Agency, with the support of the in-house NGS and IdentyPath platforms, as well as the deployment of tools for the bioinformatics analysis of genomic data, have enabled the WGS approach to be progressively rolled out for major pathogens. This action will be continued and expanded in 2023 as part of reference and monitoring activities on microbiological contaminants, following exchanges with the DGAL. Actions will be planned according to the resources available, in connection with the structuring of **bioinformatics** systems tailored to data analysis and processing, in particular with the support of the SPAAD shared service recently set up for the Laboratories for Food Safety and for Animal Health, and of the in-house NGS platform run by the Ploufragan-Plouzané-Niort Laboratory. **Metagenomic approaches and characterisation of the mobilome, resistome and pathobiome** will also be developed in the framework of research projects for studying microbial communities in complex samples (META-DETECT thesis on Shiga toxin-producing *E. coli*, MARESISTOME project using the newly developed AMR array). More generally, "-omics" type approaches will be favoured; this is why **metabolomics** studies will be undertaken in partnership with the CNAM's agri-food chair and within the METABIOT contracted unit. **Transcriptomics** work will also be carried out to understand the factors influencing the production of bacterial toxins (Estaph thesis with the CEA) and as part of a study of the immune and/or cellular response of the host subjected to different stress conditions (ProtectCamp and RIMICIA projects).

In addition, technology using **digital PCR** will be deployed and assessed in the framework of the DIGIDIAG cross-cutting project involving five of the Agency's laboratories interested in the tool, in particular for counting food pathogens (PATHODIGIT project).

Work using mass spectrometry will be developed for quantifying staphylococcal enterotoxins and detecting *Bacillus cereus* emetic toxins (ToxBt cross-cutting project in parallel with the use of cell-based assays). **The investigation of Raman microspectroscopy technology**, in collaboration with the CEA, will be pursued and assessed to determine the viability status of *Listeria monocytogenes* and *Vibrio* in workshops in the fishery products sector (VIBRATO project).

Work will continue on the molecular and cellular approaches developed in food virology to assess infectious risk. Work using cell-based assays and **impedance measurement** will be continued and applied to different viral models, including SARS-CoV-2 as part of the COVRIN project (within the One Health EJP); different potential transmission routes of the virus will be explored through the DIVA project (Digestive tropism and Intestinal pathology of SARS-CoV-2 VAriants: exploration through *in vivo* and *vitro* models) funded by the EMERGEN consortium for the faecal-oral route and the H2O SARS CoV project for the water-borne route.

National and European partnerships to improve understanding of hazard characterisation in a One Health approach

Reference activities and research work on the identification and characterisation of microbiological and biological contaminants in food will need to complement those of our partners in other sectors or ecosystems, in a **One Health approach**. To achieve this, **links with the NRCs** will be consolidated and strengthened, particularly for *Salmonella* and *Listeria*, as part of investigations of human cases and identification of food sources of contamination, and in the context of shared research to capitalise on existing biological assets and strain collections. In order to facilitate these exchanges, it will be necessary to set up the **means for sharing existing databases** while being mindful of confidentiality constraints. Specific actions to foster these closer ties will be carried out jointly with the DSP.

Research work will be encouraged with national research organisations, especially those working with ANSES through partnership agreements or which are partners on thesis topics (INRAE, CEA, Ifremer, Inserm, universities, veterinary schools, etc.).

Similarly, work in **partnership with EFSA** will be continued within projects such as EuroCigua2 (on ciguatoxins), RASCS (on contaminants in seafood) and RIMICIA (microbiomes of the gastrointestinal tract). In addition, EFSA is progressively setting up a scheme to enable the transmission by Member States and comparison of genomic data from WGS of foodborne pathogenic bacteria, in conjunction with the European Centre for Disease Prevention and Control (ECDC). ANSES will be closely involved in this European structuring of the **One Health Molecular Typing System** for surveillance and investigation of the targeted pathogens (initially *Listeria monocytogenes*, *Salmonella* and STEC), including its EURL on *Lm,* even more so since ANSES's 2022 appointment as the national coordinator for data transmission and laboratories providing data (transmission mobilising the NRLs for *Salmonella* and *Listeria*).

The research projects carried out in bacteriology, virology and parasitology within the framework of the **One Health European Joint Programme (EJP)**, coordinated by ANSES, are helping to strengthen partnerships among the 44 partners in 22 Member States working in veterinary public health, food safety and public health. Some of these projects involve integrative, pivotal actions for the future, with the provision of reference materials, harmonised methodologies or systems for analysing and centralising genomic data and metadata (OHEJP COHESIVE, ORION and CARE projects). These European collaborations may continue within the framework of the Horizon Europe programme and potentially the "Sustainable food systems" European partnership in preparation. This partnership will take a holistic approach to changes in food systems by integrating environmental and food waste aspects, which could generate emerging or re-emerging health hazards. European projects along these lines are already under way, such as the FOREWARN project on the occurrence, fate and behaviour of emerging pathogens in coastal surface waters within the framework of the Aquatic Pollutants programme, as well as the HOLiFOOD project for a holistic approach to tackling food system risks in a changing global environment, which was selected during the Horizon Europe programme's first call for proposals.

5. Laboratory activities for the antimicrobial resistance theme

Antimicrobial resistance is a major public health problem with a wide-ranging impact, involving issues of human and animal treatment, but also a threat to our ecosystems. In the animal sector, the two EcoAntibio plans deployed since 2012 (2012–2016 and 2017–2022) have achieved very significant numerical objectives for reducing animal exposure to antibiotics and the prevalence of resistant bacteria in these populations. ANSES's "Antimicrobial resistance" cross-cutting strategic theme aims to coordinate and promote synergies in the Agency's various skills on this issue, in order to provide the public authorities with the support and scientific expertise appropriate to its comprehensive approach (One Health) at the national, European and international level.

More specifically, the Agency is working on three major tasks related to its missions. These concern:

- **monitoring trends in development** of the main resistance phenotypes and identifying emerging threats in the animal, food and environmental sectors, especially with regard to uses of antimicrobials of particular importance to humans (cephalosporins, fluoroquinolones, colistin, carbapenems, etc.);
- **characterising antimicrobial resistance genes and genetic carriers** and their dissemination in these same sectors, and in an integrated approach including the human and environmental sectors;
- **monitoring animal exposure to antibiotics** through monitoring or surveys of sales of veterinary antimicrobials (carried out by the ANMV) and the associated impacts in the context of various experimental models for mathematical or biological, *in vitro* or *in vivo* studies.

Strengthening the effectiveness of our surveillance schemes

Since 2021, implementation of **regulatory analyses within the framework of the LNR's activities** has been stepped up, in line with changes in the European regulations (Commission Implementing Decision (EU) 2020/1729). It remains on an alternating annual schedule – pigs and calves in odd years (2023), poultry in even years (2024) – and focuses on the search for antimicrobial resistance of the bacteria *Campylobacter* spp., *Escherichia coli* and *Salmonella* in animals on arrival at the slaughterhouse (caeca) and during distribution (retail meat). Limited since 2016 to the species *Campylobacter jejuni* in poultry, it now includes *C. jejuni* and *C. coli* in poultry, pigs and calves.

At the same time, the Agency will continue to operate and consolidate **other antimicrobial resistance surveillance schemes** (mainly the Resapath[8] network and the Vigimyc[9] network for mycoplasmas). With regard to the Resapath network, structural changes were finalised; these fell under Action 14 of Theme 3 of the EcoAntibio 2 plan. One has helped optimise data flows (EDIR Project, EcoAntibio) allowing the number of member laboratories to be extended in 2022, while the other has finalised online access (R-Shiny) to these data. In addition, a Bayesian approach enabled the modelling of Resapath data in order to characterise changes in the susceptibility of *Escherichia coli* clinical isolates to colistin (COBAYE Project, EcoAntibio). In 2023, Resapath will continue its participation in the national meta-network PROMISE, financed since 2021 under the priority research programme on antimicrobial resistance of the future-oriented investment programme PIA3, which links together all the professional networks addressing antimicrobial resistance in the human, animal and environmental sectors. In particular, as part of this meta-network's "Surveillance" working group, ANSES is coordinating a multi-partner inter-sector project to collect French data on antibiotic use and antimicrobial resistance in humans and animals, with the aim of producing an analysis similar to that produced at European level by EFSA, the EMA and the ECDC (JIACRA or Joint Interagency Antimicrobial Consumption and Resistance Analysis).

In 2023, long-term monitoring of antimicrobial resistance will also be supplemented by the completion of **specific surveys** in project mode (surveillance in fish farming, in the marine environment or in veterinary hospitals, antibiotic resistance of mycoplasmas, resistance to colistin, etc.). More generally, these antimicrobial resistance surveillance data are of great help in assessing the effectiveness of public policies on the use of veterinary antibiotics in France. In 2023, they will continue to be compared with data from human medicine, in particular as part of the new Interministerial Roadmap (FIM) currently being prepared.

[8] Surveillance network for antimicrobial resistance in pathogenic bacteria isolated from farm and companion animals in France
[9] Monitoring network of pathogenic mycoplasmas in ruminants

At European level, in the framework of the **EU-JAMRAI** joint action (2017–2020) and on the basis of its expertise in coordinating the Resapath network, ANSES had taken the lead in the **EARS-Vet** initiative for coordinating European surveillance of antimicrobial resistance in veterinary medicine in Europe, in line with the objectives of FIM Action 39. The Agency will continue to pursue this ambition in 2023 and beyond. The past year provided an opportunity, particularly in the context of the French Presidency of the Council of the EU, to reaffirm the importance of the EARS-Vet scheme, which is now scheduled to be included on the agenda of the next joint action (**EU-JAMRAI 2**) funded by Europe's EU4Health programme. Also at European level, ANSES will contribute in 2023 to the new EU survey on the prevalence of **MRSA in pigs**.

Pursuing methodological developments for the detection of antimicrobial resistance

In 2023, the Agency will pursue several actions on **methodological approaches for monitoring antimicrobial resistance**. These actions will capitalise on previous programmes, in particular those developed within the framework of the One Health EJP (IMPART and HARMONY projects). They will include, as necessary, the update to the list of methods for conducting tests to determine bacterial susceptibility to veterinary antibiotics, following the 2019 publication by ANSES of specifications for industrial use. They will also focus on developing/standardising methods for determining susceptibility to antibiotics of more specific bacterial species/genera (*Aeromonas*, *Vibrio*, *Brachyspira*, *E. cecorum*, etc.) selected for their clinical or epidemiological importance, the lack of study methods, or their relevance as indicators of antimicrobial resistance in certain environments (ARMANI project, EcoAntibio 2). Lastly, the Seq2Diag project, funded under the Priority research programme on antimicrobial resistance and seeking to better predict the phenotypic resistance of bacteria from their genomes, will continue.

Better characterisation of the resistome and antimicrobial resistance gene flows

In 2023, the laboratories will continue their work on **molecular characterisation of the resistome and of genetic carriers of antimicrobial resistance determinants in different environments**. As such, the Agency has been involved in several research projects funded by the EcoAntibio 1 and 2 plans, the latter of which will come to an end in 2023. This work will also be continued or finalised as part of ongoing European projects such as PRE-EMPT (One Health EJP), or funded or co-funded by ANSES (MASTOC and CARAVANE projects). Similarly, the DYASPEO project (2021–2027), funded under the Priority research programme on antimicrobial resistance, seeks to characterise these genetic flows between pets and humans. Interventional approaches to control the flow of antimicrobial resistance are also planned (for example, in chickens, the ENVIRE project funded by the Joint Programming Initiative on Antimicrobial Resistance – JPIAMR). All these studies enable assumptions to be put forward on the spread of antimicrobial resistance and possibly on source attribution between animals within sectors, between sectors at national level and/or cross-transmission with humans. These interdisciplinary programmes also enable synergies to be developed with many other partners working on the antimicrobial resistance issue (INRAE, Inserm, *Santé Publique France*, *Institut Pasteur*, other institutes in Europe, etc.), as part of an integrated approach. In this respect, the ABRomics project to set up an interoperable One Health multi-omics platform, financed under the Priority research programme on antimicrobial resistance (of which ANSES is a partner), will enable our laboratories to contribute to the intersectoral (human, animal, environment) analysis of WGS data for antibiotic-resistant bacteria.

Refining our understanding of the links between exposure and impacts

The emergence and spread of antimicrobial resistance results from the exposure of individuals and ecosystems to external factors, mainly but not exclusively antibiotics. For antibiotics, the role of **co-selection** will be investigated (ICONIC project, JPIAMR). Cross-linkages with the use of biocides may also be important, and the **impact of disinfectant biocidal treatments** (enzymatic detergents, antimicrobial materials) on microbial ecology and resistance mechanisms to biocides, metals and antibiotics will continue to be studied. In particular, the adaptation of bacterial biofilms to biocides and the consequences on antimicrobial resistance will be studied in 2023 as part of an ANSES-INRAE thesis (BioCARe project) and an ANR-JCJC project (BAoBAb). In connection with the ANMV's activities, the laboratories will help refine quantification of animal exposure to antibiotics through surveys on use. Work will also be finalised or carried out to assess, through experimental approaches and/or overall molecular

analyses (metagenomics, for example), the impact of antibiotic use on the microbiome, on the emergence of cross-resistance mechanisms and on the overall microbial ecology of ecosystems (METARes, STAFILMS, CANIBIOTE, CONTALIM and EMOXIMINT projects). As a follow-up to the ANSES report on alternatives to antibiotics published in April 2018, work on the relevance of credible alternatives to antibiotics (bacteriocins, algal hydrolysates, pre- and probiotics, phage therapy, autogenous vaccines) will be finalised in 2023 (RESPEC, CANIPHAGE, EVASION, EcoAntibio 2 projects).

Strengthening cross-cutting links between the Agency's laboratories and assessment departments

The laboratories are developing work on the topic of antimicrobial resistance in conjunction with other specialist ANSES divisions or disciplinary fields other than those usually covered. Following the same approach as for the work in its expert appraisal on the risks associated with antimicrobial resistance in environmental media initiated in 2018 by the Risk Assessment Department, whose conclusions were issued in 2020 and which included a contribution from the ANSES laboratories, a formal request initiated in 2021 on the **analysis of priority antimicrobial resistance risk profiles** (bacteria/resistance phenotype pairs) from the animal sector and of importance for public health will be finalised in late 2022. More generally, all the interface work carried out over the last few years between laboratories and assessment departments will provide input for the debates on the construction of the EcoAntibio 3 plan in 2023, within the framework of a renewed interministerial roadmap. Lastly, 2023 will see the finalisation of a trans-disciplinary doctoral study combining technical expertise from the biological sciences with a reflexive and conceptual contribution from philosophy and the human and social sciences around issues related to ethical and socio-cultural aspects of the fight against antimicrobial resistance in livestock.

Strengthening the Agency's international position on antimicrobial resistance

In 2023, the Agency will continue its support to the FAO under its **mandate as FAO Reference Centre for antimicrobial resistance**, which was awarded to ANSES in November 2020. The Agency will contribute to the four themes developed by the FAO in its plan to combat global antimicrobial resistance by mobilising all of its expertise. For example, the Agency will participate as needed in the drafting of guidance documents on the appropriate use of antibiotics and control of antimicrobial resistance, or may provide support for strengthening the laboratories' analytical capacity. As such, a project awarded under the EcoAntibio plan (REFFAO, EcoAntibio 2) was launched in 2022 to conduct an inter-laboratory test on antimicrobial resistance in African countries, similar to what is done in the Resapath network. Under its FAO mandate, ANSES is also involved in setting up the FAO's InFarm database on antibiotic use and antimicrobial resistance. Other measures, including training, will also be discussed in 2023 as part of this mandate, as well as in collaboration with the ENSV-FVI veterinary school, and will include sociological aspects. ANSES's partnership with the Mérieux Foundation further strengthens this international positioning on antimicrobial resistance.

6. Laboratory activities for the epidemiology and surveillance theme

The ANSES units working in epidemiology:

- provide scientific and technical support to the supervisory authorities, partner organisations and ANSES's risk assessment departments, in particular on Category A,D,E diseases under the European Animal Health Law;
- jointly coordinate several surveillance schemes (Resapath, Vigimyc, *Salmonella*, RNOEA, Resumeq, foot-and-mouth disease rapid-response unit);
- provide support to the Agency's national reference laboratories, enabling them to carry out their tasks of collecting, processing, facilitating access to, transmitting and disseminating epidemiological surveillance data (Order No 2015-1242 of 7 October 2015 on the organisation of surveillance concerning animal health, plant health and food safety);
- are involved in the three national epidemiological surveillance platforms (animal health, plant health and food-chain safety) in the coordination teams, operational teams and working groups;
- make a significant contribution to the production of articles for the *Bulletin Epidémiologique* on Animal Health & Nutrition published jointly by ANSES and the DGAL, in particular the annual health reviews on the surveillance of regulated diseases in animal health, and the monitoring and control plans for food-chain safety;
- conduct their own research activities.

In 2023, they will again offer major scientific and technical support and carry out key research on Category A,D,E diseases, in particular avian influenza, but also foot-and-mouth disease, tuberculosis and brucellosis. In addition to this vital groundwork, ANSES's other key epidemiological work for 2023 will focus on improving surveillance methods and methodological research.

Modelling of avian influenza and foot-and-mouth disease

In addition to surveillance, which is an ongoing activity, the epidemiologists at ANSES devote themselves to studying the spread of zoonotic diseases/agents and other hazards in populations and ecosystems. This is designed to both predict their spread and measure the impact of management measures.

On the topical issue of highly pathogenic avian influenza (HPAI), the use of network and spatial models will improve the study of disease transmission and the effectiveness of both surveillance protocols and control measures. The inclusion of socio-economic factors will help produce more realistic predictions.

In the same vein, but on the subject of foot-and-mouth disease, the EuFMD has made a disease transmission model available to its member countries in order to simulate the spread and control of the disease. In 2023, this model will be adapted for France in order to assess the needs for designing the control scheme (size of the vaccine bank, human resources, etc.).

Epidemiology of tuberculosis and brucellosis

The descriptive and analytical epidemiology of bovine tuberculosis will be studied in depth, particularly in relation to wildlife, with a particular focus on:

- the spatial structuring of *Mycobacterium bovis* infection in badgers in the enzootic area;
- the feasibility of injectable vaccination of badgers as a complementary measure for controlling bovine TB in the most infected areas.

Brucellosis will also be researched. A field survey will provide an estimate of the seroprevalence of canine brucellosis in France and be used to study the risk factors for infection. Through thesis work, the transmission of bovine brucellosis in Ecuador and Paraguay will be analysed using dynamic models.

Improving surveillance methods

In a context where it is more vital than ever before to monitor diseases in animal and plant health, in addition to food-chain safety, there is a constant need to look for new ways to improve monitoring and make it more efficient. The research carried out by the teams of epidemiologists at ANSES seeks to propose new surveillance and alert methods. For example, they rely on syndromic surveillance, which enables near-real time monitoring of non-specific health indicators such as mortality, movements, demographic data or requests for analyses. Application of artificial intelligence tools, with the use of new machine learning and deep learning approaches, will be increasingly common, to improve the analysis of time series, for example.

Assessing surveillance is also an essential part of its improvement, and further development of assessment tools will be on the agenda for 2023. These tools include a One Health assessment component of surveillance, to ensure that all the compartments involved (human, animal, plant, environment) are taken into account.

Methodological research

Alongside studies targeting the understanding of a disease or pathogen, it is important to develop new epidemiological and modelling tools and methods in order to better explore population health. To this end, the use of phylodynamic tools will be extended in order to build models combining epidemiological and genetic data, and to gain a better understanding of pathogen transmission. Methodological developments will be carried out to quantify the impact of biases in input data.

7. Laboratory activities for the exposure to and toxicology of chemical contaminants theme

With a view to reducing the impact of chemical contaminants on human health, animal health and the environment, the "Exposure and toxicology" cross-functional strategic theme helps promote cooperation and fosters collective debate in the Agency's core divisions. By coordinating the European Partnership for the Assessment of Risks from Chemicals (PARC), which creates a broad European network for cooperation between risk assessment entities and organisations in charge of research and reference activities, the Agency will continue its efforts to contribute to an integrative strategy for toxicological risk assessment by strengthening our ability to detect and characterise hazards, assess exposure, and monitor and control these hazards. Launched in May 2022, this partnership is one of the elements of the European Union's Chemicals Strategy for Sustainability. ANSES is in charge of the scientific and administrative coordination of this partnership, and many related projects and activities will be implemented in the Agency's laboratories. The complementarity of these activities will be developed with the risk assessment and surveillance activities carried out as part of its reference missions.

Major health issues identified, studied and pre-empted

Several reference mandates for chemical contaminants of anthropogenic (**veterinary drugs, plant protection products**), natural (**marine biotoxins, histamine**) or combined (**trace metal elements and nanoparticles**) origin in food, hive products and water have been entrusted to the Agency's laboratories. They will therefore continue to develop and validate analytical methods, contribute to standardisation, organise inter-laboratory tests and coordinate laboratory networks under quality assurance.

With regard to **veterinary drug residues**, the reference work carried out under Commission Implementing Regulation (EU) 2021/808 will lead to a review of all analytical methods being launched. A new surveillance programme based on the use of high-resolution mass spectrometry for some samples will be implemented. New methods covering substances common to the regulations on pesticides and veterinary medicinal products will be validated according to common principles. Methods for analysing highly polar compounds and perfluoroalkylated substances (PFASs) in water will be developed. In synergy with their reference mandates, the laboratories are continuing research to develop novel analytical approaches to characterise new hazards in food and water. Data on contamination levels are thus being produced through exploratory measurement campaigns and will be useful for ongoing or future risk assessment processes at the French and European levels.

In order to provide updated data on the levels of exposure of the French population to substances alone or in mixtures, several units of the ANSES laboratories will work with the Risk Assessment Department to carry out the Third Total Diet Study (**TDS3**).
Work on antibiotic pharmacology will be carried out in connection with the revision of dosages in veterinary medicine.

Technological and methodological innovations currently being integrated

As part of their cross-functional work and in conjunction with the European PARC partnership, the laboratories are continuing their collaborations on the use of **high-resolution mass spectrometry** for developing broad-spectrum analysis protocols, in terms of substances screened for (multiple classes), signal processing to screen for known (post-target analysis) or unknown (non-targeted analysis) substances, and the creation of virtual sample libraries.

In order to contribute to hazard characterisation and to the reduction of animal experimentation, studies of toxicokinetics and toxic potential (cellular toxicity, genotoxicity, endocrine disruptors, neurotoxicity) of substances belonging to different classes (toxins, nanomaterials, microplastics, pesticides) will be characterised within the framework of several national or European projects via regulatory or new methodological approaches. Several of these studies are being carried out during pre-validation of tests for endocrine disruptors.

8. Laboratory activities in other areas

Besides the activities presented above, within the Agency's six cross-cutting strategic themes, the ANSES laboratories may be required to carry out certain research or reference work in other areas. One key example is development of the Nancy Laboratory for Hydrology's activities on wastewater and sewage sludge matrices, as part of its new mandate as NRL for SARS-CoV-2 monitoring in these matrices, entrusted to the Water Microbiology Unit. In this respect, we will continue to set up the SUM'EAU network for detection of the viral genome in wastewater, in order to help monitor virus circulation in the population.

Regulated Products Division

The division's main task is **scientific assessment** and **decision making (at national level)** for products and active substances (ASs) included in the following thematic areas:

- **Plant protection products** (PPPs);
- **Biocides**[10];
- **Fertilisers and growing media**;
- **Veterinary medicinal products (VMPs)**.

Assessments cover the **risks to human or animal health and the environment**, but also the **effectiveness**, selectivity or expected **benefit** of using a product, depending on its type.

The division's scientific teams also make **various other contributions to ANSES's in-house expertise** in broader fields (animal health and biocides, ecotoxicity issues, etc.). Units of the Regulated Products Division are involved in **preparing dossiers under the REACH[11] and CLP[12] Regulations.** Other cross-cutting tasks, such as the expert appraisal for setting maximum **residue** limits (active substances of VMPs and PPPs), are also vital ongoing activities. Lastly, the teams are very active in improving assessment methodologies, for both internal and external work, most of it at European level.

The 2023 work programme of the Regulated Products Division will be structured around the following framework elements:

- **Continue improving** the **efficiency observed in 2021–2022**, by looking for ways to optimise assessment and decision-making processes to help achieve appropriate examination times for applicant dossiers, in particular in the area of plant protection products; this goes hand in hand with maintaining efficiency when the indicators are already highly satisfactory (case of veterinary medicines);
- **Maintain responsiveness** for **work on formal requests**, particularly in the event of alerts issued by the bodies responsible for the requests, while striking a balance with work on application dossiers, the division's core activity;
- **Continue digitising internal and external procedures** and update (or consolidate) the information systems, in a context of urbanisation of the Agency's information systems and in keeping with the European tools used by ECHA, EMA and EFSA;
- Respond to the priorities and challenges facing society, in line with **major government plans and national, European or international issues:**
  - Support the **National Biocontrol Strategy**;
  - Provide input for the debate on **Ecophyto 2+ by contributing to this plan's Scientific and Technical Committee** (Science for Expertise Division) and to questions on the determinants of its indicators;
  - Be a stakeholder in **EcoAntibio** through the help of the ANMV[13] in preparing the Third EcoAntibio plan, or its participation in the interministerial committee for health in connection with the roadmap for controlling bacterial resistance to antibiotics;
  - Contribute to the **Pollinator Plan;**

[10] Including swimming pool water treatment products and embalming products in the transitional period of Regulation (EU) No 528/2012. For these two themes, see the 2022 document on transfer of missions to ANSES.
[11] REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) is a European regulation (Regulation (EC) No 1907/2006) that came into force in 2007 to secure the manufacture and use of chemicals in European industry.
[12] Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures (known as the CLP Regulation).
[13] French Agency for Veterinary Medicinal Products, within the Regulated Products Division.

- Contribute to the **National Endocrine Disruptor Strategy (SNPE)**: ANSES will continue assessing the endocrine-disrupting nature of chemicals within the framework of the SNPE2. For biocidal and plant protection active substances, ANSES will assess or contribute to the assessment of dossiers: this will systematically include assessments of substances' endocrine-disrupting properties;
- Update methodologies in the context of the EC's Chemicals Strategy for Sustainability, the European deliberation on "One substance, one assessment" issues.

- **Strengthen information sharing and maintain listening and dialogue**, in particular by perpetuating the **platform for dialogue** on marketing authorisations for plant protection products;
- Maintain an **activity and presence at the European and international level** in the bodies and priority work of the European Commission, EMA, EFSA, ECHA, UN Food and Agriculture Organization (FAO), World Health Organization (WHO), World Organisation for Animal Health (WOAH, formerly OIE), European and Mediterranean Organisation for Plant Protection (EPPO), Codex Alimentarius joint UN/WHO programme, etc.

This programme is divided into five themes, described below.

1. Maintain an appropriate response for assessing products and active substances and authorising products within the Regulated Products Division's remit

An appropriate level of taxes and budget path:

The division's speciality and major challenge remain its work to assess the risks and effectiveness/benefits of various products on the basis of applications from companies holding or applying for MAs or similar authorisations[14].

This activity is mainly financed by **tax revenues or fees**, which depend on the volume and nature of applications submitted. A major issue is therefore the appropriate level of taxes and tax rates, in view of the costs borne by the Agency. After revising the tax rates for VMPs and for certain dossiers relating to fertilisers and growing media, the division will continue to work with the Legal Affairs Department on the tax rates for PPPs and to examine the Regulated Products Division's business model **with a view to achieving multi-year stabilisation**.

Adjustments to the information systems:

Modernisation and digitisation through information systems (ISs) will contribute to overall efficiency. To this end, in the area of biocides, the **SIMMBAD platform** will be replaced by a new version that will be operational by early 2023 (with a major effort to reach the target in late 2022 due to its role in the reporting of data by firms). An **information system specific to biocides**, which complements the European R4BP online reporting system, is also planned and under construction. This involves a sustained effort by the teams of the core departments (DAMM and DEPR[15]) and the IS department of the Regulated Products Division, which has an impact on some of their other work. The **D-Phy** project is in production for the digitisation of application forms concerning plant protection products, and will be further developed to eventually include a tool for managing the submission of application dossiers. The European **PPPAMS**[16] project will be closely monitored to align potential European obligations on PPPs with existing in-house tools, in order to improve cooperation and efficiency, and avoid duplication of tasks and tools. Lastly, software applications relating to veterinary medicinal products now exchange data with the European databases developed by the EMA under the new Regulation (EU) No 2019/6, since its entry into force on 28 January 2022, with the creation of the UPD (Union Product Database). It is a **major achievement to have implemented these flows in a timely manner with the deadline for the regulation's entry into force and the particularly large volumes of exchanges for France. It will be supplemented by other developments** (data on manufacturers/wholesalers, management of online sales reporting, etc.).

[14] Parallel trade permits; authorisations by mutual recognition, etc.
[15] Regulated Products Assessment Department and Market Authorisations Department within the Regulated Products Division.
[16] Plant Protection Products Application Management System https://food.ec.europa.eu/plants/pesticides/authorisation-plant-protection-products/pppams_en

Prioritisation of dossiers and reduction in processing times:

Dossier assessment and decision-making activities (concerning both active substances and products) continue to **vary in volume** depending on European activities (re-assessment of ASs or assessment of new ASs) and the renewal of MAs, as well as the submission of other applications including new MAs, parallel trade permits (PTPs), etc. For 2023, in addition to the significant expected workload related to reporting on the active substance glyphosate, the following points should be noted:

- **Trajectory for biocontrol products on track:** this **priority, which has already been largely achieved**, has resulted in improved timeliness and therefore a reduction in the number of dossiers currently being examined, limited processing times (shorter than the European legal requirement) and around one hundred applications processed per year since 2017;

- **Backlog reduction trajectories maintained for PPP dossiers including parallel trade permits, and processing times maintained or improved** for all regulated products.

Milestones in the 2023 expert appraisal trajectory:

- **Buffer zones to protect residents**: the 2023 trajectory for PPPs will be marked by the consequences of the scheme to **update certain MAs to include "safety distances for residents" (i.e. nearby residents and bystanders present** by chance when PPPs are applied) whose safety must be guaranteed. ANSES put in place an adapted procedure allowing the submission of applications by 1 October 2022, followed by a risk assessment with a view to updating, in the corresponding MA decisions, the safety distances for local residents regarding products classified as Category 2 CMR (carcinogenic, mutagenic or reprotoxic substances), at the request of the ministries as part of the revision of the amended Ministerial Order of 4 May 2017, following a decision by the Council of State. This scheme led to a **peak in activity concerning admissibility, assessment and decision-making, and the reporting of specific data to the Ministry of Agriculture**.

- **Methodological developments and scientific cooperation**: in this respect, it is worth noting the strong dimension of the work on methodological developments in the field of **plant inputs and biocides**, with a **full agenda including more than 50 internal and external collaborative projects**. Given their European collaborative nature, these projects are included in Chapter 5 of this summary.
  One key point is cooperation with EFSA in the field of cumulative risk assessment (CRA) associated with dietary exposure to pesticides under the "EFSA-SANTE Action Plan on CRA for pesticides residues" programme, in which eight to 15 organ systems require a CRA, or ANSES's involvement in the European Partnership for the Assessment of Risks from Chemicals (PARC) co-financed by Horizon Europe. These initiatives seek to improve the understanding of risk assessment methodologies for chemicals.

- For veterinary medicinal products, a priority is to reinforce expertise for the assessment of **new therapies in veterinary medicine**: use of stem cells, immunotherapy (RNA vaccines, interleukins, monoclonal antibodies, etc.) and phage therapy. **The strategic issues in the coming years, which will be addressed if necessary in cooperation with the French Health Products Safety Agency, mainly concern:**
  - Phyto- and aromatherapy;
  - Phage therapy: participation in the drafting of assessment guidelines;
  - "Innovative" therapies such as monoclonal antibodies and emergency vaccinology (mRNA vaccine, technological platforms);
  - External antiparasitics with the topics of resistance and environmental risk (follow-ups to the formal request on external antiparasitics in the form of baths, showers or sprays), and risks for the user (in spot-on formulations).

Milestones in the decision-making process:

It should also be noted that, as a decision-maker, ANSES also has to perform essential tasks that are unrelated to expert appraisal, such as **disseminating decisions, informing regulated product users about decisions (MAs, PTPs), or shedding light on regulations** when they have an impact on applications or the form of the decisions. In this respect, the following should be mentioned:

- Management of the consequences of the new provisions on **protection of bees;** safety distances for residents regarding CMR2 products, with dossiers to be accepted in 2022 and processed in 2023 and beyond;
- Decisions published by maintaining and updating the **E-Phy website** (responses to requests, publication of news, especially on product withdrawals, making the database more reliable);
- Improved availability of data to the public (open data) with more complete files and weekly updates;
- Any PPP containing a banned co-formulant must be withdrawn (withdrawal of the MA) or reformulated (modification of the composition, **so that no prohibited co-formulant remains** in the PPP) as soon as possible and before the legal deadline of 24 March 2023 set at European level. This work will therefore be completed in 2023, with the last few dossiers relating to certain reformulations (minor changes in composition);
- The coming year will also be marked by the DAMM's analysis of the conclusions of the expert appraisal on **plant protection products containing the active substance copper** and by decisions being made, in a complex context that will take into account the comparative assessment already carried out and any substitution options, with a socio-economic perspective provided by the Social Sciences, Economics & Society Department (DISSES);
- Information on amendments to adapt national laws and regulations on veterinary medicinal products to European regulations.

2. Securing the authorisation system through post-MA monitoring and the response to emerging issues

Vigilance schemes: phytopharmaco-, veterinary pharmaco- and toxicovigilance

Using the results of studies promoted and financed under the phytopharmacovigilance scheme (PPV, Science for Expertise Division), as well as signals from other vigilance schemes, and its interactions with SpF, the French Biodiversity Agency (OFB) and other partners, ANSES will pay close attention to **various health signals related to uses of regulated products**, detected mainly through clinical cases and epidemiological studies (cohorts, case-controls, etc.) or through biological, regional or environmental monitoring studies.

The PestiRiv study launched in 2021–2022 (sample collection) will continue.

ANSES's work will also focus on **improving knowledge in the following areas, by supporting various studies** conducted through phytopharmacovigilance activities. Signal processing (similar to the work performed in 2022, for example, on prosulfocarb) will continue, with signals being **classified as alerts** where necessary. **Potential measures can be taken on MAs if warranted due to the risk**, like the amendments made on S-metolachlor in 2022, for instance.

In the field of veterinary medicinal products, the above-mentioned new regulation laid down the implementation of a **new approach to veterinary pharmacovigilance**, through the establishment of **signal detection**: the ANMV in particular has positioned itself as a driving force for proposals through its continued participation in the European pilot working group on signal detection, but also more broadly through its contribution to European signal detection and the implementation in France of regulatory or communication actions decided on at European level.

For all active substances, other work conducted outside the Regulated Products Division under the **toxicovigilance** scheme, with the support of the working group on "Toxicovigilance for regulated products", will also enable **data on poisoning cases associated with regulated products** to be analysed and taken into account when issuing, amending or withdrawing marketing authorisations. As an illustration of the interactions between vigilance and expert appraisal activities, the inventory work conducted on cases of poisoning by biocides provided input for the formal request on the "ban on self-service sales of certain categories of biocidal products", an opinion on which was published in late 2022.

Monitoring committees and post-MA actions:

Following the renewal of their **members in 2022**, the MA monitoring committees will continue their work on **adaptation, feasibility and compliance with risk management measures in the MAs for PPPs and biocides**. For VMPs, **the mandate of the members of the corresponding Monitoring Committee (CSMV) has been extended for two years until September 2024**: a review of its activity and a call for applications to ensure it can continue its work under appropriate conditions will be launched in early 2024.

Inspections:

In the area of monitoring and control, ANSES will continue to regularly offer its expertise on plant protection products to State control bodies.
It will also carry out **inspections of product formulation facilities** in line with its resources (one FTE) and prerogatives (Article L. 250-2, 5 of the French Rural and Maritime Fishing Code).

The ANMV's inspection mission will continue with the following related work in particular: integration of a **new inspection policy for new facilities or activities** subject to the obligations of Regulation (EU) No 2019/6 or the French Public Health Code, through a 2023 inspection programme based on risk analysis; continuation of the European-wide review of **good manufacturing practices** for veterinary medicinal products and autogenous vaccines; participation in the European working group on **good distribution practices**; adoption of new guidelines for **good laboratory practices**.

3. Maintain expert appraisal activities in response to formal requests

In addition to its main tasks examining authorisation applications or assessing active substances, the Regulated Products Division will work on responding to formal requests, with lead times adapted to both its own constraints and those of its supervisory authorities or other requesting bodies.

The division contributes to various projects led by other Agency entities whenever its expertise is useful and can be mobilised, such as in the following work:

- **Relevance of PPT active substance metabolites** in water intended for human consumption; on **relevant metabolites** in water, the work of the Risk Assessment Department (DER) will continue according to the priorities of the Directorate General for Health (DGS), with a view to documenting reports received on the presence of certain metabolites in water analysed by the PPV scheme (a recent example being S-metolachlor). In a similar vein, the cross-cutting work of other units (on TRVs, health reference values, blood contamination limit values) contributes to the division's response to various formal requests and to the analysis of reports detected by the PPV scheme;
- Request for an opinion on the development of a **calculation method to assess the overall criticality of health and environmental hazards associated with the use of household products** intended for consumers, in order to clarify their labelling;
- **Bedbugs (scientific support for updating the governmental control plan);**
- Management measures in the event of **botulism** in wildlife (biocidal issues);
- Analysis of the contribution made by the results of the **"Pesticides are in the air!" study** (*Générations Futures* association), in order to define buffer zones to protect local residents;
- **Stinging caterpillars**: health risk analysis/management recommendations;
- Actions in the area of animal health **(disinfection on farms**);
- Support for the **Vectors Mission with regard to vector control methods**;
- Establishment of **resistance monitoring;**
- etc.

The main expert appraisals led by the division are as follows:

- **Exposure to succinate dehydrogenase inhibitors (SDHIs)**: by early 2023, ANSES will finalise its expert appraisal on SDHI fungicides. The Agency will issue opinions on its assessment of the cumulative risks to consumers associated with fungicidal substances containing succinate dehydrogenase inhibitors via food, and **on the revision of toxicity reference values for the main SDHI active substances**. At the request of the expert group, the deadline was extended in 2022.

  Moreover, the first phase of a study funded by the phytopharmacovigilance scheme on the impact of environmental exposures on tumour risk in subjects at risk of hereditary SDH-related paraganglioma, conducted by teams from the Paris Public Hospital System (AP-HP) and Inserm, was followed by the launch of the second phase, also financed by ANSES and included in the PPV budget for 2023.
- **External veterinary antiparasitics in the form of baths, showers and sprays**: the ANMV will publish the results of the internal request it has been working on since 2020, on assessing the risks to human health and the environment in ruminant herds.
- Essential oils and plants of interest for **phytotherapy and aromatherapy in food-producing animals: the opinion issued in 2022 will lead to further developments on maximum residue limits (MRLs) in interaction with ANSES's working group on "Plants".**
- **Methodological guide on the release into the environment of non-indigenous macro-organisms** beneficial to plants.
- **Insecticide resistance in mosquito vectors:** after having proposed guidelines for monitoring mosquito resistance to insecticides throughout France (ANSES 2021), ANSES will issue an opinion in early 2023 on strategies for the use of biocidal products in inter-epidemic and epidemic situations.

4. Strengthen information sharing and maintain listening and dialogue

Improving access to information on regulated products, whether for applicants or stakeholders, will continue to be a **priority** for the Agency.

In view of the extremely high societal expectations regarding regulated products, and PPPs in particular, the Agency will pursue its cross-cutting objective of **openness to society, in line with its undertaking in the renewed Charter on Dialogue and Openness to Society**, with regard to all its stakeholders. This will mainly take shape through the maintenance of the **platform for dialogue on plant protection products**, set up in 2017, which will continue its exchanges two to three times a year under the chairmanship of Mr Bernard Chevassus-au-Louis. It facilitates discussions on the results of expert appraisals and the Agency's work, and enables better training and information to be provided for all stakeholders.

In terms of **transparency, the assessment conclusions and MA decisions for PPPs, fertilisers and growing media[17] are published** on the ANSES website. The regular publication of a **monthly MA newsletter** also helps improve access to information on these activities. ANSES will continue in this vein by regularly upgrading the E-Phy website to integrate user feedback, and continuing to make data available as open data.

The ANMV will organise its **fourth ANMV Day for stakeholders** representing the entire veterinary medicinal products chain, from veterinary pharmaceutical manufacturers, wholesalers and veterinarians to breeders, in the fourth quarter of 2023.

5. Maintain and develop the RP Division's activity and presence at the European and international level

The Agency will continue to be at the forefront of European and international issues.

Cooperation in assessments:

This concerns application dossiers processed at European level (**European MAs for biocides and VMPs, or zonal MAs**, depending on the situation and the products concerned) or processed on behalf of European agencies in the framework of **reporting for ASs**[18] of biocides, VMPs and PPPs. ANSES will continue to hold a leading position in Europe among rapporteur Member States for **assessing active substances or setting MRLs for PPPs and VMPs**. With dossiers for which it is not the rapporteur Member State, it will play an active part in the **comment and peer-review phases**. The Agency shares the opinions it publishes with the other Member States.

Support for its supervisory ministries:

ANSES **supports the competent authorities in preparing for regulatory and standardisation bodies or discussion groups and negotiations**, at European (SCoPAFF[19]) and international (CCPR[20]) levels for plant protection products; in the BPC[21], CG[22] and meetings of the competent authorities and the SCBP[23] for biocidal products; through participation in EPPO's[24] herbicide panel; and in the EMA's standing committee on veterinary medicinal products (CVMP[25]) and expert group on veterinary medicinal products (CMDv[26]) for veterinary medicines.

[17] Reports and decisions regarding MAs for biocidal products are also published, but on the ECHA website.
[18] Active substances
[19] SCoPAFF: Standing Committee on Plants, Animals, Food and Feed. A regulatory committee chaired by the European Commission
[20] CCPR: Codex Committee on Pesticide Residues
[21] BPC: Biocidal Products Committee, under the European Chemicals Agency (ECHA)
[22] CG: Coordination Group for Biocidal Products, for which ECHA provides the secretariat
[23] SC: Standing Committee on Biocidal Products
[24] EPPO: European and Mediterranean Plant Protection Organisation
[25] CVMP: Committee for Veterinary Medicinal Products
[26] CMDv: Coordination Group for Mutual Recognition and Decentralised Procedures – Veterinary

It also supports the competent authorities in **setting standards for fertilisers or preparing and negotiating delegated and implementing acts under the Regulation on veterinary medicinal products**.

The ANMV will continue its **involvement in the implementation of the new European regulation** on veterinary medicinal products by providing scientific and technical support to its supervisory ministries with the negotiation of delegated and implementing acts for the new Regulation and the adaptation of French law.

Cooperations, in particular relating to changes in methodological frameworks:

ANSES continues to be proactive in the field of **assessment methodologies** for all regulated products. **EFSA, EMA and ECHA are and must remain key partners** for all the Agency's work in the field of regulated products, particularly to ensure a collegial approach to expert appraisal, knowledge sharing and methodological harmonisation.

In order to better promote its scientific knowledge and publications, ANSES will remain closely involved in developments relating to methods for assessing the effectiveness and risks of products regulated **at European level**:

- **Cumulative risk assessment in the context of MRLs for PPPs** (EFSA);
- Development of methodologies for assessing **dietary exposure** (ECHA's ARTFood Working Group – Assessment of Residue Transfer to Food);
- European Working Group on **Antimicrobial resistance** (ECHA, European partners);
- PERIAMAR (PEsticide RIsk AssessMent for **Amphibians and Reptiles**);
- Participation in the EFSA group on revision of the guidance document on the risk assessment of **plant protection products and bees**;
- Participation in the EFSA group on revision of the guidance document on risk assessment for **birds and mammals** (PPPs);
- Participation in the group on development of **toxicokinetic/toxicodynamic (TK/TD) approaches and modelling in ecotoxicology** for PPPs;
- Participation in the group on development of **groundwater** risk assessments based on spatial distribution modelling for PPPs;
- **Critical appraisal tools for evaluating ecotoxicity studies** (with European partners in the Netherlands and Germany);
- Biocides: participation in the **development of methodologies and tools for assessing human exposure** to chemicals;
- Biocides: participation in the development of **environmental assessment methods for disinfection by-products**.

This list is not exhaustive and there are also other national studies, as well as close cooperation on **assessing the effectiveness of PPPs**.

ANSES will pursue essential development work through its participation in the scientific work planned under the European PARC partnership.

In the field of veterinary medicinal products, ANSES will also maintain or develop a major presence in European bodies, mainly by strengthening its role through positions as chairs and vice-chairs of European groups (such as the **chair of the CMDv**, for which it obtained a second mandate in 2020) and by continuing its commitment to the network of **European Heads of Medicines Agencies (HMA)**.

Through its mandate as a **WOAH Collaborating Centre** in the field of veterinary medicinal products, the ANMV will continue its deep commitment to **combating antimicrobial resistance**, in particular by setting up the WOAH database and training national focal points in different countries. The ANMV will be a driving force in **EMA working groups**: the Antimicrobials Working Party (AWP), work on the New Veterinary Regulation (banned antibiotics or those whose off-label use is restricted, data collection), and also in the monitoring of antibiotic use at European level via contributions to the ESVAC scheme (European Surveillance of Antimicrobial Consumption) led by the EMA and to actions on **resistance to antiparasitics**.

The ANMV will also work on the **environmental risk of external antiparasitics in the form of baths, showers or sprays and the user risk assessment (URA) for spot-on treatments**, a subject that is expected to be pursued with an EMA working group.

It will also do its best to continue providing assistance with development and sharing French expertise through the various cooperation agreements, particularly with third countries.

Science for Expertise Division

In line with the strategic orientations by thematic area on the one hand, and implementation of the early stages of the 2023–2027 goals and performance contract (COP) currently under negotiation on the other, the work programme of the Science for Expertise Division is based on the set of work sheets drafted by its entities (drawing on cross-functional links within the Agency), in conjunction with its supervisory ministries and external partners. This summary documents the teams' commitment to health and safety. Without being exhaustive, it gives some perspective to major actions that contribute to increasing the efficiency and scientific robustness of ANSES's work, advancing major projects in the various specialist areas, preparing and supporting developments in response to health and societal challenges, enhancing institutional communication on the Agency's role, challenges and importance, and integrating its work at the European and international level. The choices here have been made for their illustrative nature, as the division's activities flow from the entire work programme. In addition, for the communication and international parts, they concern the division's contribution to ANSES's overall work in these areas.

1. Improving efficiency and increasing the robustness of our work

Although the next version of ANSES's goals and performance contract (COP) is still under development, improving efficiency (Theme 5 of the current COP) will continue to be high on the Agency's agenda. The same applies to the implicit requirement for its work to be robust (through its scientific excellence, quality and independence – Theme 1 of the COP), as this is an essential condition for its credibility. In essence, achieving these goals relies on the contribution of a broad range of activities, measured by aggregate indicators. This is the case, for example, of compliance with contractual deadlines for formal requests (indicators 5.3.2 a/b/c of the COP), or the robustness of the process for analysing personal interests of the members of our expert groups.

With regard to deadlines, the quality indicators for 2021 showed a return to the situation prior to the severe pandemic period in 2020 (which had a noticeable impact), with even an improvement being noted. The coordination teams are currently conducting a cross-cutting analysis of the feedback from this "forced experiment" in conducting all activities remotely. Their work is examining both **organisational aspects and the technical equipment in the meeting rooms used for collective expert appraisal work**, in order to prepare – in conjunction with the teams of the Technical Affairs & IS Department – an investment enabling hybrid meetings with high-quality sound and video, which will favour the inclusion of remote participants. In addition, the extranet platform for publishing documents intended for expert appraisals has changed, with the adoption of the government's RESANA platform. This should help generalise the co-authoring processes that speed up the integration of comments in the final phases of expert appraisals.

Following the finalisation of a report by ANSES's Scientific Board proposing a **roadmap for greater integration of the principles of the exposome in the Agency's work**, a deployment action will accompany its implementation (Sheet 5.8.6) over different time frames. Besides the expert appraisals that have benefited from advice from the Scientific Board's working group, an examination of the programme reveals a greater number of activities that are directly in line with this rationale, such as the formal request on the additivity of different types of dust in the workplace (Sheet 4.4.7), or the internal request on identifying effective solutions for limiting exposure to cadmium, taking multiple exposure contexts into account (Sheet 1.8.5), which will also draw on the work carried out in the PARC project, and lastly the debates undertaken by the DISSES with different units of the DER on the socio-economic and demographic determinants of different categories of exposure (Sheet 7.1). Teams from the division and beyond will be mobilised on another major deployment plan, resulting from the work of the ACCMER working group to standardise and generalise the recommendations of the Agency's Scientific Board on taking the weight of evidence and uncertainty into account (Sheet 5.8.3).

Another methodological task for the division will be the creation (for new missions) or updating (where they are obsolete) of various assessment guidelines. **The drafting of such guidelines** is a major technical investment by the Agency in the context of internal requests. Its usefulness is motivated by **the importance of defining and sharing relevant data** with the economic players concerned by dossier submission **to ensure that ANSES's expert appraisals are conclusive**. Indeed, postponed deadlines or dossiers for which a negative conclusion is reached due to a lack of data are a waste of time and resources for everyone. In 2023, such work will be undertaken in the following areas: assessment of the risks of release of different types of GMOs (Sheet 5.8.7), assessments of the risks associated with trials of feed additives (Sheet 2.1.2), assessment of the microbiological effectiveness of processing aids (Sheet 1.2.1), and guidelines for the assessment of water treatment products and processes (Sheet 1.5.2).

Still on the topic of methodological activities, the DISSES's work programme sheet on socio-economic analysis (Sheet 7.1 "Supporting and developing expertise in social and economic sciences") shows that this activity will cover topics that encompass ANSES's five areas of activity. As a common thread, the DISSES will endeavour to identify the methodological elements for capitalisation that are essential for progress in this field, in the course of its work and with the support of the Expert Committee on "Socio-economic analysis".

Lastly, regarding the ranking of food safety hazards and risks, ANSES has begun work in response to an internal request to **develop and implement the results of the proof of concept provided in the request – responding to the Interministerial Committee for the modernisation of public administration –** in the context of the PrioR sheet (1.8.6). This will also interface with work carried out by the epidemiological surveillance platforms of the Research & Reference Division.

To improve the management of its activities and in response to the expectations expressed by ANSES's supervisory ministries in connection with the new COP, ANSES will propose a **revision of the expert appraisal protocol** that defines the relationship between ANSES and its sponsors **for emergency formal requests**, in order to adapt it to the changing context and to diversifying support needs. Another growing need for these sponsors is to obtain answers to questions covering an increasingly vast field, sometimes exceeding the scope of ANSES's work, as was the case with the recent request for an opinion on the assessment of the public health impacts of the fox population (mentioned in Sheets 1.3.5, 2.4.4 and 7.1), which required close cooperation with the French Biodiversity Agency (OFB). In order to facilitate the implementation of inter-agency/inter-institute work involving separate expert appraisal processes, ANSES will propose a draft cooperation protocol.

Data governance and strategy will rank highly among the goals of ANSES's future COP. In 2023, therefore, the division will contribute to the preparation of an integrated strategy that will address both the data generated by the Agency's activities (in connection with its platforms, observatories and studies) and the need to access data for expert appraisals. Following on from the work already undertaken, it is worth highlighting that carried out in connection with Sheet 5.6.3 (MADIMS: Provide internal and external users with methodological information and data useful for risk assessment), which also includes **ANSES's participation in and contribution to the "Green data for Health/GD4H" group of the PNSE4,** supported by the Ministry of Ecology's General Commission for Sustainable Development (CGDD). Because data issues concern all of ANSES's areas of activity, the question of **occupational health** databases is also addressed by an action described in Sheet 8.1.6, which extends, within the fourth Occupational Health Plan, the work of the multi-partner group examining the complementarity of five French data-collection schemes through work on topics identified as sensitive.

Lastly, due to its budget being stable overall, the research funding activity is even more concerned by efficiency and robustness actions, given the high expectations that had been raised by the PNSE4 for environmental health research. Coordination of the PNR EST (Sheet 9.3.1) will therefore continue to contend with changes in the funding it can mobilise for its calls for research projects (budgeting of the IFER tax since 2019, funding of dedicated calls on endocrine disruptors – EDs, and exceptional allocation of the proceeds of penalties on air quality). In this respect, following implementation of their shared portal, ANSES is continuing its cooperation with the ANR, which in 2023 will include efforts to harmonise practices and the opening of a user space and a directory of experts (to assess projects). The latter could also be useful for extending ANSES's talent pools. **The link with expert appraisals will continue to be supported**, for better consideration of the recommendations of expert appraisals in the shaping of research questions.

2. Initiating or completing major projects

Of all the different topics involving several entities within the division, or extending beyond it to include other ANSES entities, this summary highlights the following projects:

Promotion of a joint ANSES/*Santé Publique France* methodology: In the 2018 framework agreement between *Santé Publique France* (SpF) and ANSES, the project to jointly conduct the next general population survey, following those carried out separately for the INCA 3 and Esteban studies, was one of the priority cooperation actions between the two agencies. In order to jointly collect scientific data demonstrating the links between individual, dietary and environmental determinants and population health, ANSES and SpF therefore outlined a single survey. This ambitious tool will enable both agencies to fulfil their missions and the goals of the national plans, while offering innovations enabling data exploitation and cross-referencing and the production of useful indicators for monitoring the effectiveness of public policies in the areas of health, food and the environment.

From a scientific point of view, this major national joint survey will enable collection of the data needed to carry out both agencies' missions with regard to food, nutrition, biomonitoring and health monitoring. Besides the sharing of the survey tool, the other major innovation being tested is the transition from a periodic system (deployed every 5 to 7 years) to a continuous one, in order to more closely monitor societal changes, some of which have become very rapid.

For the research funding activity, another major project was initiated in late 2022 and will be completed in 2023. This is the periodic assessment of the National Research Programme for Environmental and Occupational Health (PNR EST), the research funding scheme run by the Agency. The previous exercise was conducted in 2017, under the aegis of the Scientific Board. For this edition, given the maturity reached in managing the call for proposals, the preferred angle for this assessment is the usefulness for public policy-making, in particular through the contribution to scientific, public health and occupational health issues. This assessment should therefore help position the PNR EST scheme, and its strengths and weaknesses, in relation to other research funding mechanisms, both from the point of view of the players (benefits, attractiveness for research teams) and of the sponsors (contribution to missing data, methods, or alerts on a broad range of health issues). The question of the financial dimension of the projects supported, in relation to the goals and the scope of funding, will also be examined. This invaluable information will help the Agency and its supervisory bodies identify ways to give this programme a renewed dimension.

Another of ANSES's major projects is its **contribution to national thematic plans being renewed: in environmental health with the PNSE4 "My environment, my health"; in occupational health with the National Occupational Health Plan (PST4), which has been officially launched; the Second National Endocrine Disruptor Strategy**, which will be redefined or extended; in nutrition and health with the National Nutrition and Health Programme (PNNS); a cross-cutting approach in support of the French National Cancer Institute (INCa) for the new strategy to fight cancer, etc.

In addition, as part of the orientations being set for the future COP, the division is particularly focused on preparations to receive new missions at ANSES – subject to final decisions. The aim is to work on integrating the responsibilities for cosmetics and tattoo products currently assigned to the ANSM, in both our vigilance and assessment missions. At the request of several ministries, a debate is also being held with the French Scientific and Technical Centre for Construction (CSTB) on establishing a cooperation arrangement to carry out the various tasks of the Indoor Air Quality Observatory, which could evolve in its ambition to become an Indoor Environment Quality Observatory.

Furthermore, the division considers that the following major projects should be started or completed, depending on the case, when implementing the 2023 work programme:

- Expert appraisal work on bedbug control and prevention, including an analysis of the benefits and possible risks associated with the different control methods available, as well as a socio-economic analysis of the impacts of bed bug infestations, will be finalised in the first half of the year (Sheet 3.3.2);
- An analysis of the socio-economic impacts of changes in the regulatory framework for using plant protection products containing copper and the identification of chemical and non-chemical alternatives, which follows on from the 2021 report on the mapping of uses of PPPs containing copper, is expected in autumn 2023 (Sheet 7.1). This action is being carried out with the Regulated Products Division;
- Production of work on new genetic engineering techniques (directed mutagenesis or cisgenesis techniques) potentially in several stages given the breadth of the field covered (Sheet 5.8.7);
- Completion of the formal request in occupational health on cleaning workers, who are subject to a high degree of multiple exposure (Sheet 4.4.1);
- Initiation of an expert appraisal by ANSES on the basis of a formal request from the Ministries of Health and Ecology on the risks associated with exposure to substances in the PFAS class (scope and terms currently under discussion mean that no work sheet is currently available).

3. Implementing the necessary changes to address new health or societal challenges

The division is fully involved in revisiting and scaling up ANSES's actions with stakeholders thanks to the establishment of the new Social Sciences, Economics & Society Department (DISSES) (Sheet 7.2). In addition to setting up a new "Biotechnology, Environment and Health" dialogue committee, **the DISSES is considering how to organise the dialogue between ANSES and its stakeholders** in order to improve the existing mechanisms, while of course listening to their views. The new perspective of the recently appointed chairs of the three dialogue bodies could also contribute to this. In addition, **the Agency will strengthen its interactions to support other players, in particular the French Economic, Social & Environmental Council (CESE) and even the National Consultative Ethics Committee (CCNE)**, with two complementary perspectives: support them in their debates by sharing the results of our expert appraisal work, but also by relaying the concerns and questions raised in our committees, which refer to subjects within their mandates.

Meeting societal expectations also means **initiating expert appraisals in response to formal requests from stakeholders**: in 2023, an expert appraisal will be conducted following a formal request from the *Générations Futures* association. Its analysis will involve the division's Phytopharmacovigilance Unit and the Regulated Products Division. As numerous formal requests were received from occupational health stakeholders in 2022, efforts in the coming year will focus on pursuing this work.

To meet societal challenges, the division **conducts work on cross-cutting issues that underlie societal transformation**: circular economy and changes in consumption patterns, climate change and biodiversity, consideration through the exposome of multiple exposure sources and substances, and changes in society's attitudes to animal welfare. For many reasons, 2022 was marked by special circumstances that brought home to the population the reality of the limits to our resources in different areas: energy, food and water. This is of course a reason for ANSES to be ever more attentive, but also an opportunity to get the population to listen more closely to its recommendations.

With regard to *climate change and biodiversity*, considerable attention will be paid to work on vector control (Sheet 3.3.3 and 3.5.1) in order to adapt the strategy and tools for monitoring and control to changes in the areas where vectors are established, as well as to work on assessing the probability and socio-economic impact of arboviruses. In this same context, the Agency hopes to have room for manoeuvre in its workload regarding water-related risk assessment, in order to begin responding to the internal request on the ranking of health hazards affecting drinking water production due to climate change (Sheet 3.4.4 for an internal request featured in its work programme since 2020). In terms of overall assessment, in relation to biodiversity, it is worth reiterating the above-mentioned formal request on the assessment of the public health impacts of the fox population (see § 1 above).

In terms of *responding to changes in consumer expectations and behaviour*, ANSES will initiate work in 2023 on updating nutrition recommendations for school canteens (Sheet 1.4.3) and, after numerous exchanges in the thematic steering committee (COT) on dietary health and with the ministries, a formal request on characterising and assessing the health impacts of consumption of ultra-processed foods (Sheet 1.4.5). The internal request discussed with the COT on animal health in June 2021, which seeks to propose a scientific framework for practices that are developing in response to societal demand concerning animal welfare labelling (Sheet 2.4.1), will enter a second phase in 2023 after publication of an initial report. Similarly, the work begun in 2022 as part of Action 3 of the PNSE4, on a calculation method to assess the health and environmental hazards of household products, will continue in 2023 after an initial report in late 2022 (Sheet 3.2.9). Lastly, following on from its expert appraisal of the health impact of light emitted by LEDs, ANSES will undertake a specific study of toys containing them by examining the new version of the EN 62115 standard, applicable since February 2022, in order to ascertain its suitability in relation to the identified risks and the specific sensitivity of children (Sheet 3.1.2).

Anticipating emerging threats and risks is one of the major themes of the current COP (Theme 2), which will be included in the COP under preparation and will be supplemented by a section on preparedness for emergency or crisis situations.

The data collected by the various vigilance schemes led by ANSES, under the coordination of the Health Alerts & Vigilance Department (DAVS), and through the activities of the epidemiological surveillance platforms to which the Research & Reference Division's laboratories contribute, already represent an important source of **identification of emerging threats**.

A major focus in 2023, for all activities – vigilance, epidemiological surveillance and risk assessment (Sheet 2.2.3) – will of course be the development of the avian influenza situation. Vigilance is a source of great mobilisation, both to support the ministries in managing an animal epidemic that has moved from a seasonal to an endemic phenomenon, and to adapt control measures. This vigilance needs to be stepped up to address the changes and mutations the virus is likely to undergo if it jumps between different animal species, whether wildlife or domestic livestock. Maximum attention must be paid to identify any mutation that could transform this epizootic virus into a zoonotic virus, transmissible to humans and capable of human-to-human transmission.

In addition, concerning the vigilance schemes, the DAVS will make full use of the new working group on "Emerging risks in occupational health" of the National Network for the Monitoring and Prevention of Occupational Diseases (RNV3P), while ensuring the close involvement of the network's partners, particularly via its steering committee (Sheet 8.1.3). With regard to developments made to carry out non-targeted data mining (Sheet 8.1.4) by automatically detecting signals (syndromic surveillance, monitoring of chronological trends in poisoning by certain agents, data mining), the priority for 2023 will be to prepare feedback to be shared both internally at ANSES and externally with agencies conducting similar development work.

With regard to phytopharmacovigilance (Sheet 5.6.1), 2023 will be an opportunity to deploy the new strategic framework, whose development has led to it being postponed and its time frame extended to cover the period 2023–2028. Deployment continues **of two major studies supported by PPV: Pesti'loge, which is the pesticide measurement component of the second national housing campaign (CNL2), and PestiRiv**.

In addition to a component on emerging threats, the future COP will also include explicit expectations on ANSES's contribution to preparations for various emergency or crisis situations. In 2023, this will take the form of internal coordination at ANSES, involving both the DAVS and the laboratories of the Research & Reference Division, to organise mobilisation and exchange networks in preparation for the major sporting and media events of the 2023 Rugby World Cup and the 2024 Olympic Games. This coordination is closely tied to the mechanism set up by the ministries.

Lastly, following on from its involvement in the Committee for Open Science (CoSO) and by giving some context to all the work carried out within this framework, the division aims to produce an initial "open science barometer" under the aegis of the DFRVS. This will also mobilise the division's other entities and ANSES more broadly.

4. Contribution to communication measures and institutional relations

Communication and institutional relations are generally addressed at Agency level, but some actions are managed by the division's entities or call heavily on their resources, in accordance with the general orientations for this field. For 2023, this mainly involves the following:

1. Continuing to support and contribute to the in-depth reflection and actions on risk information of the Department of Communication and Institutional Relations (DICORIS), by increasing efforts in connection with more reflective work, and with scientific press such as "The Conversation";
2. The Paris International Agricultural Show (SIA), to be held in physical form in early 2023, will also engage the division's teams;
3. In conjunction with the DICORIS, continuing to promote PNR EST-funded work, in order to maintain its visibility and attractiveness;
4. Increasing the visibility – and therefore the effectiveness – of the Agency's vigilance missions requires the professionals most concerned to take on board the messages and alerts resulting from the work of the vigilance schemes.

5. Europe and international

These actions are generally coordinated within ANSES by the European & International Affairs Department (DAEI) and are in line with Theme 3 of the COP orientations. Some of them are managed by the division's entities or call heavily on their resources, in accordance with the general orientations. In 2023, our European action will be characterised by two main themes.

The first is the translation into various EU texts of the strategic orientations of the European Green Deal. By way of illustration, next year should see the entry into force of a CLP (classification, labelling, packaging) regulation including new hazard classes, in particular for the ED hazard, and various new classes in ecotoxicology in order to better characterise the way in which certain substances subsist in the environment, either by accumulating or, on the contrary, proving to be highly mobile. Similarly, a change in the REACH regulation should also follow in late 2023. Each time a draft text is produced, ANSES's scientific teams are called on to analyse the relevance of the proposed provisions with regard to health issues.

Obviously, the entry into force of these completed regulations will subsequently be factored into the work carried out to support the French authorities for the various regulations to which ANSES contributes: REACH, CLP, Biocides, etc. (Sheets 5.2.3 to 5.2.10).

The second major component will be the start of the fully operational phase of the European Partnership for the Assessment of Risks from Chemicals (PARC). Launched in May 2022 following its validation by the European Commission, its goal is to provide chemical risk assessors and risk managers with new data, knowledge and methods, and to develop the network of specialist players and the scientific skills required to address current,

emerging and new challenges in chemical safety. The Science for Expertise Division, and in particular the DER, will be involved in different work packages as WP/task leader or contributor, and will also seek to inform the project governance of any strategic needs and priorities for the development of methods or knowledge.

In addition to the PARC partnership, the division is also likely to be involved, albeit to a lesser extent, in other partnerships being set up in ANSES's field, whether in sustainable food or animal health and welfare.

In more generic terms, the division's European and international activities are reflected in three main types of work: (i) joint work combining the efforts of ANSES with its European counterparts in a specific field; (ii) research in which the teams may be leaders or contributors; and (iii) recurring work with the major European agencies in line with the scope of our national missions.

Regarding work in partnership with our European counterparts, it is worth mentioning two European Joint Actions, co-funded by the European Union's Third Health Programme, for which ANSES is the lead French entity (with other partners such as *Santé Publique France*, French National Cancer Institute and the DGS):

- Launched on 1 October 2020, the Best-ReMaP Joint Action on implementation of validated best practices in nutrition, with the DER leading the monitoring of reformulations of processed products at European level, has been an opportunity to share and compare the OQALI practices implemented in France for many years now. It will come to an end in 2023, with the production of a set of deliverables (Sheet 1.7.5);
- Currently being implemented, the second joint action to assist European countries in the deployment of the Tobacco Products Directive (following on from the Joint Action on Tobacco Control, JATC).

Lastly, the division actively contributes to structured cooperation with the European agencies in its field of activity, namely EFSA, EEA and ECHA.