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ANSES 2024 work Programme

Adopted by the Scientific Board
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Investigate, evaluate, protect

1. GENERAL ORIENTATIONS

The 2024 work programme is part of a renewed strategic framework for ANSES, with the convergence of three key elements: the adoption of its new goals and performance contract signed with its supervisory authorities for the period 2023–2027 (COP 2023–2027); a proactive process of reflection initiated by the Agency in order to rethink its action, in a context where the different effects of climate change are becoming more apparent every day; and a growing belief that a "One Health" approach is both essential and sustainable in developing adaptation and mitigation solutions for our planet.

Identified as an underestimated factor in the origins of the COVID-19 pandemic and also seen in other emerging threats, the perception of the importance of a comprehensive approach to health – One Health – has never been so acute, even if we have yet to develop an understanding of what it represents in real terms. Promoted as early as the 2000s by the World Health Organization (WHO), it recognises that the health of humans, domestic and wild animals, plants and the environment in general are all interlinked, and that the health of each one depends on all the others. This is a real 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. It is referred to extensively in the various sections of this programme – both the scientific orientations for each area of activity and the summaries of the divisions – and mentioned very explicitly in the titles of several strategic themes of the Agency's COP.

Even though the Agency's broad scope is naturally positioned to sustain and develop such an approach, ANSES believes it necessary to identify and **support a core group of partners, who are essential if we are to act fully in One Health mode**, and with whom we can strengthen links and joint actions. This will begin with *Santé publique France*, whose agreement with ANSES will be renewed in early 2024.

Moreover, the notions of sustainability and climate change impact are becoming concrete realities for a large part of the population and of stakeholders: tensions over water, energy and certain products are being clearly felt and have been exacerbated by particularly acute climate events (intense heat, prolonged drought, extreme climactic events). These realities are measured in terms of both individual and collective consequences, which in turn raise awareness and lead to appropriate action.

It is therefore more than ever necessary to shed light on the issues at stake and the risks involved, so that these growing concerns can prompt action on the underlying causes by guiding measures designed to mitigate and adapt to climate change. For the Agency, this will require a number of changes: broadening the parameters and factors we take into account in our work, and even opening up our methods to prospective studies based on scenarios, whereas risk assessments tend to be based on retrospective assessments. To address this need for change, ANSES has initiated a **debate**

with its entire management team on how to take account of climate change. This will be **rolled out across the board via the seven scientific directors**.

At the same time, **the costs of risk remediation** – whether health, climate-related or environmental – are leading to greater account being taken in public policies on health and risk of **prevention** and as a prerequisite, the sharing of adequate information for the proper handling of the risk factors. One of the Agency's responses to this issue is the development over time of reference standards for socio-economic assessment in the various contexts in which it operates.

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. Among the evolving or emerging European policies of interest to the Agency, ANSES has identified the ongoing revision of the Framework Directive on ambient air quality and the establishment of a Soil Framework Directive; these concern environments in and through which the risk factors associated with substances and pathogens can potentially accumulate over the long term. It is particularly important to take account of these historical accumulations, which are largely due to the pressure of human activities on the environment, as their effects may be exacerbated by new abiotic stresses (water stress, temperature, hazards).

Against this context and within its missions, ANSES's response is built around three themes:

1. Pursue and amplify the Agency's know-how, which echoes these challenges, while ensuring that it is supplemented by complementary know-how and setting out a clear data strategy;
2. Increase vigilance, in particular by interlinking schemes and data, and foster anticipation through research and emergency preparedness;
3. 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. It also means ensuring that it is supplemented by complementary know-how, particularly from key partners. At the intersection between the One Health concept and the exposome approach, the aim is to further analyse the interactions between risk factors of all kinds: pathogens, hosts (wild or domestic animals, animals or humans), environments and contaminants.

This must lead us to strengthen our capabilities and practices for assessing the impacts and risks of the environment on human health. These approaches will be all the more useful in situations where there is high uncertainty and a lack of information, to help better anticipate crises and underscore the benefits of prevention. The other imperative is to **focus work on action priorities and allocating efforts**, faced with the proliferation of sources of risk. Preventive action in environmental health should systematically draw on rational, structured analyses based on data, which are first debated and then prioritised.

Two new conditions have been identified for the amplification of know-how: capitalising on synergies between risk assessment and epidemiological approaches, and **taking advantage of big data** in order to develop a data strategy, as called for by our COP 2023–2027. While ANSES already processes epidemiological surveillance data in animal and plant health as part of its missions, with the support of INRAE[1], the strategy for bringing together toxicological and epidemiological approaches in human health **requires a change in scale**. **This change will involve bringing together data processing systems that currently communicate little or not at all**: between big data on human health (available via the SNDS[2]) and environmental data, which are also very abundant (although less so in some areas, such as indoor air). Cross-referencing with databases from other sectors (social data) is another useful approach, especially since the exposome also needs to take the social component into account.

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, and 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.

[1] INRAE: French National Research Institute for Agriculture, Food and the Environment
[2] SNDS: National health data system

Increasing vigilance and fostering anticipation means first of all working to interlink vigilance, surveillance and data analysis systems, which is another component of the data strategy. Continuing to strengthen cooperation between national reference laboratories (in animal health or food safety) and national reference centres (in human health) is essential, driven by ANSES and SpF[3] between ANSES's reference laboratories, in order to promote the joint use of data (convergence in the analytical production of data, data exchanges, etc.), particularly for epidemiological investigations during health events.

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 is also reflected at ANSES by the development of 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 ability to bring together and exploit different datasets from a variety of sources (human, animal, environmental, etc.) with a view to integration also depends largely on how their production is envisioned and planned as far in advance as possible, with an all-encompassing and holistic view. In this respect, a research strategy for the integrated production of scientifically relevant and robust knowledge and data needs to be rethought to ensure that it directly addresses the challenges of the One Health policy, in a truly coherent "science to policy" approach. In view of this need, **the Agency, with the support of its supervisory ministries, is working to overhaul the PNR EST** in a national context that is currently undergoing a review of research planning.

At European level, ANSES is **an active participant** in the preparation, deployment and closure **of major European projects**. On the strength of its experience in leading the European Partnership for the Assessment of Risks from Chemicals (**PARC**), for which it is ensuring the work's contribution to public policy, the Agency is now committed to starting up the animal health and welfare (**AHAW**) partnership, and is seeking continuity solutions for the very productive work of the One Health European Joint Programme (EJP), which finishes at the end of 2023.

Lastly, fostering anticipation means preparing for organisational modes geared to emergencies or planned large-scale situations such as major sporting events, including the 2024 Paris Summer 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.

[3] SpF: Santé publique France

Developing our contributions to risk governance means first of all consolidating the new missions inherited from the previous COP (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 Act4) and preparing for the missions whose assignment to ANSES has been confirmed by the 2023–2027 COP (vigilance and assessment relating to cosmetics and tattoo products, contribution to supporting the Indoor Environment Quality Observatory with the CSTB5).

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 questions of an increasingly global nature. It also means deploying socio-economic assessment components more frequently, in line with our COP goals, in order to enhance the results and insights provided to risk managers.

To better play its role in risk governance, ANSES is reviewing the way it interacts with stakeholders, in order to assist them more effectively in the transitions to come. In 2024, the Agency will have the opportunity to build on work carried out under the leadership of the new Social Sciences, Economics & Society Department (DISSES) on the organisation of dialogue between ANSES and its stakeholders.

It is essential to use the contributions of ANSES's different activities to shed light on the profound changes to come, particularly those due to climate change, and this will largely be achieved by continuing the various dialogue interfaces it has established and consolidated since its founding.

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, welfare and nutrition, environmental health, plant health and protection, and occupational health. Although presented by area, their implementation often requires cross-cutting efforts between the teams carrying out the Agency's work.

A number of orientations per area of activity are based on the national plans in which ANSES has a leadership role or to which it contributes (PNSE4, SNPE2, PST4, PNNS, EcoAntibio, Ecophyto2030, etc.).

Consistency in the implementation of these orientations is also down to the work of ANSES's cross-functional scientific directors in seven fields – food safety, epidemiology & surveillance, antimicrobial resistance, exposure to and toxicology of chemical contaminants, plant health, animal health & welfare, and occupational health.

Setting out these general orientations by area of activity, the summaries prepared by each operational division detail the main projects for 2024, showing the main themes by action. These

[4] ASAP: Act for the acceleration and simplification of public action

[5] CSTB: French Scientific and Technical Centre for Building

include actions sheets for the functional departments devoted to international action and to communication.

The 2024 work programme shows that all ANSES's missions and activities specifically take full account 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:

1. continue acquiring knowledge to support expert appraisals;
2. contribute to the development of scientific methods and tools to better detect and assess risks, and enhance them with socio-economic assessment components;
3. anticipate, identify and characterise health risks, including in times of crisis;
4. develop an increasingly integrated approach to risk assessment in support of the One Health approach;
5. prepare during 2024 a data strategy for all ANSES's activities.

With the growing need for insights into health issues, in 2024 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.

2. STRATEGIC ORIENTATIONS

Food safety and nutrition

Background

Food safety and issues of nutrition are major societal challenges due to their health and economic consequences; they are a central concern to many citizens, who have high expectations for healthier and more sustainable food.

Implementation of **the French EGAlim Act**[6], 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 be **"healthy, safe and sustainable"**, covering all these dimensions from production through to consumption. **While environmental factors must be considered**, other topics also need to be taken into account, such as **food waste** or **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.

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 the fundamental, life and health sciences, as well as 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 this context, ANSES strives to remain a reference scientific player in **assessing the health and nutritional risks and benefits of food**, by maintaining the highest standards, a forward-looking and integrative capability, and an openness to dialogue, as well as active participation in European and international work.

[6] 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)

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 "-omic" approaches more broadly, and detecting markers of interest to public health associated with the virulence, antimicrobial resistance, toxicity or infectivity of these 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.

New monitoring data will be generated from 2024 onwards, increasing the volume of analytical data. This will require the implementation of a strategy and infrastructure to enable their computerised storage, accessibility, interoperability and reprocessing. Work to structure data of all types, along with the associated metadata, should enable a "big data" management policy to be put in place and methods such as machine learning to be used to analyse these data. It should also gradually integrate socio-economic data, in interaction with the teams and competencies in these areas.

The surveillance platform for the food chain, coordinated by ANSES jointly with the DGAL[7] and INRAE[8], 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.

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[9] and Esteban[10] 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 INCA studies.

Anticipate new risks and trends to ensure evolving and integrated assessments

The methodology for tomorrow's risk assessments will require the development of knowledge on and greater consideration of aggregate exposure and exposure to mixtures of several substances. In

[7] DGAL: Directorate General for Food within the Ministry in charge of agriculture
[8] INRAE: French National Research Institute for Agriculture, Food and the Environment
[9] INCA: French Individual Survey on Food Consumption
[10] Esteban: Health Study on the Environment, Biomonitoring, Physical Activity and Nutrition

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. The European PARC[11] programme 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 and risk assessment, as well as 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 GMOs[12] 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 and health crises. 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.

[11] PARC: European Partnership for the Assessment of Risks from Chemicals
[12] GMO: Genetically modified organism

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[13], 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 communities of other research organisations (INRAE, CIRAD[14], CEA[15], Ifremer[16], Inserm[17]) 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[18] and FLI[19] (Germany), DTU-Food[20] (Denmark), RIVM[21] (Netherlands) and ISS[22] (Italy), and internationally with the FDA[23] (USA), Health Canada and CFIA[24] (Canada), NIFDS[25] (South Korea) and SFA[26] (Singapore).

The already very active and close collaboration with EFSA[27] 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

[13] PNNS: National Health and Nutrition Programme
[14] CIRAD: French Agricultural Research Centre for International Development, working for the sustainable development of tropical and Mediterranean regions
[15] CEA: French Alternative Energies and Atomic Energy Commission
[16] Ifremer: French Research Institute for Exploitation of the Sea
[17] Inserm: National Institute of Health and Medical Research
[18] BfR: Bundesinstitut für Risikobewertung (German Federal Institute for Risk Assessment)
[19] FLI: Friedrich-Loeffler Institut (German federal institute for animal health research)
[20] DTU-Food: DTU National Food Institute
[21] RIVM: National Institute for Public Health and the Environment
[22] ISS: Istituto Superiore di Sanità (Italian National Institute of Health)
[23] FDA: Food and Drug Administration
[24] CFIA: Canadian Food Inspection Agency
[25] NIFDS: National Institute of Food and Drug Safety Evaluation
[26] SFA: Singapore Food Agency
[27] EFSA: European Food Safety Authority

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 research and cross-cutting projects supported by the One Health EJP[28] 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 seven-year framework programme provides new tools for strengthening 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, and the one on Animal Health and Welfare, accepted in 2023, in which ANSES has a particularly strong leadership role within the European working group tasked with its coordination, other partnerships that contribute to the EU's Farm to Fork Strategy for a healthier and more sustainable EU food system, are being set up and are of major strategic interest to ANSES. These include 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 will be responding to calls for projects on food safety aspects.

[28] EJP: European Joint Programme

Animal health, welfare & 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, encompassing humans, animals and the environment. This has been clearly illustrated by recent health crises such as COVID-19, swine influenza, avian influenza, West Nile virus infections, 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, animal health, welfare and nutrition stakeholders 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 selection and spread of 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: new health hazards, especially through arthropod vectors whose range is expanding in our part of the world; 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; impact of climate change on animal health and welfare according to the production method.

These background points generate challenges that the Agency must take into account in its activities and in the establishment of its work programme in the area of animal health, nutrition and welfare.

Challenges

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

The lessons learnt from the major health crises of recent years (COVID-19 as a disease that can be shared with animals, avian influenza and its adaptation to mammals, as well as the spread of African swine fever in Europe and the emergence of epizootic haemorrhagic disease) 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.

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 approach), health monitoring and methodological support, without forgetting methodological innovation in epidemiology and modelling. These various activities form part of the anticipation of health crises, with the goal being to predict spread as accurately as possible in the event of an introduction and to anticipate management decisions, by assessing the impact of various measures using simulations. It is also worth noting the integration of socio-economic components in work to model the spread of avian influenza or African swine fever, thus bringing the human and social sciences on board in ANSES's research programmes.

Regarding **monitoring of antimicrobial resistance**, in 2024 the **Resapath** network will continue its participation in the national meta-network PROMISE[29], which links together all the professional networks addressing antimicrobial resistance in the human, animal and environment sectors. In addition, on the basis of its expertise in coordinating the Resapath network, ANSES will continue leading the European EARS-Vet[30] initiative to coordinate European surveillance of resistance in veterinary medicine, for which funding by the European EU4Health programme has now been acquired.

[29] PROMISE: Professional community network on antimicrobial resistance
[30] European Antimicrobial Resistance Surveillance network in Veterinary medicine (EARS-Vet)

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 our laboratory teams' immediate and engaged response 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**.

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, brucellosis monitoring), and through emergency collective expert appraisals when required by current events (animal epidemics such as avian influenza and African swine fever, or industrial accidents that could potentially contaminate animal feed).

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. One of the challenges 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. This mobilises **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. The discovery of an outbreak of **tuberculosis in goats in Haute-Corse** (Corsica) has led to research and risk assessment in order to better characterise transmission of the disease within a very specific multi-host system. Responses to other **formal requests** are on the risk assessment work programme for 2024, **involving all or some of the three pillars of the One Health concept: animals – humans – environment**. Among other things,

they intend to assess the risk of botulism in relation to wildlife, or of brucellosis at the interface between wildlife and domestic animals in the Bargy and Aravis massifs, and produce risk maps for tick-borne encephalitis in France.

This same One Health approach is 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.

Lastly, the importance of **vector-borne diseases** in the expected health consequences of climate change has led ANSES's laboratories to devote a large part of their work programme to **research on these infectious diseases, some of which are zoonotic** (Crimean-Congo fever, West Nile, Usutu), and on **pathogen-vector interactions** (such as the exploration of the tick immune system, the vector competence of mosquitoes), while using **epidemiology**, **citizen science** and **risk assessment to characterise vector-animal and/or vector-human interfaces** (risk mapping). The 2024 risk assessment work programme therefore includes **several formal requests on vector-borne diseases**, particularly zoonotic ones. Cross-sectoral approaches with human health and vector monitoring will be at the heart of ANSES's approach to surveillance and research into these diseases.

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.

Several ANSES teams (in reference, research, risk assessment, assessment of veterinary medicinal products) have devoted a significant part of their work in 2023 to developing a strategy for vaccinating farmed ducks against avian influenza for the 2023–2024 season. The follow-up to this unprecedented operation will continue to occupy our teams throughout 2024, as they will be watching for the development of any infection by a highly pathogenic influenza virus, within a vaccinated population in France.

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 trichinellosis in pigs or tuberculosis in badgers).

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, new vaccine strategies against foot-and-mouth disease and African horse sickness).

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**, or the identification of new drug targets and therapeutic approaches against helminths, parasites that are increasingly resistant to antiparasitic compounds.

Indeed, 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 fungi to parasites.

Better knowledge of the spread of animal diseases in order to adapt control measures is also an orientation included in the research and risk assessment 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, analysis of phylodynamic tools, contact networks and the study of transmission chains.

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. This work could be extended to include bats and rodents in 2024.

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**.

In terms of antimicrobial resistance, the co-exposure of bacteria to different products is also a field of research and investigation. Work on cross-linkages with the use of biocides will continue in 2024.

Animal welfare: i) study new livestock farming methods through an integrated approach, and continue research on relevant indicators of animal welfare in farming; ii) improve animal welfare in experiments

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**, using multi-criteria approaches. 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 responses**. 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.

In addition, expert appraisal work on guidelines for establishing animal welfare labelling standards for animal products will continue in 2024: after establishing general guidelines, regardless of the species, the expert appraisal will focus on work devoted to a particular animal species.

Lastly, the Agency will continue its efforts to **improve animal welfare in experiments**, by enriching the living environment in animal models, leading to the revalidation of experimental protocols in these new contexts. These animal models also enable the Agency to validate **alternative models** that can then be used to reduce the need for animal testing (tests on organoids, *in vitro* screening of antiviral substances, etc.).

Adapt the Agency's work to a changed regulatory environment

For the French Agency for Veterinary Medicinal Products (**ANMV**), efforts will continue on **implementing the new Regulation** (EU) 2019/6 on **veterinary medicinal products**: i) continuation of regulatory work to adopt secondary legislation at the EU level; ii) continuation of work to adapt national law; iii) 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 orde to implement improvement opportunities.

For the **NRLs and EURLs** (national and European reference laboratories), work will continue on adapting reference activities to the new regulatory context arising from **implementation of the Animal Health Law** (Regulation (EU) 2016/429 on transmissible animal diseases).

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 **animal nutrition**, work on the guidelines for the **assessment of application dossiers on particular nutritional purposes** (Regulation (EU) 2020/354) will continue into 2024.

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.

Increase ANSES's visibility through European and international undertakings

The Agency will continue working with its European partners on the **European partnership on animal health and welfare (PAHW)** in the framework of **Horizon Europe**. This European partnership was recently accepted by the European Commission and now becomes the keystone of European research in animal health and welfare for the next decade.

Lastly, the work planned for 2024 by the various laboratories holding **European** (7 mandates in animal health and welfare) **and international reference mandates** (26 WOAH[31] and FAO[32] 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 Anses 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.

[31] WOAH: World Organisation for Animal Health
[32] FAO: Food and Agriculture Organization of the United Nations

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 the environment through water, air or soil quality, or noise and artificial lighting. This impact is largely the consequence of human activities: demographic growth and its territorial distribution, industrialisation, urbanisation, the development of insufficiently controlled technologies, or unsustainable consumption patterns. Climate change, which has a major influence on the environment, ecosystems and biodiversity, is also a key parameter to consider in risk assessment.

Assessing health risks associated with the environment 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 to control them can be identified.

In addition, expert appraisal work and support for research on risks that have generated lively scientific debates and major social mobilisation 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 by 2027 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 in line with the priorities set out in its new Goals and performance contract (COP)[33] (2023–2027):

1. **Anticipate emerging threats and risks** associated with changes to the environment and climate that are sources of scientific and societal controversy (in agreement with Theme 2 of the COP).

[33] COP: Goals and performance contract – Contrat d'objectifs et de performance

2. **Improve expert appraisal practices** (in agreement with Theme 1 of the COP) 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 fully in the European "One substance, one assessment (OSOA)" initiative.
   - Promote the re-use of data generated or used in expert appraisals in environmental health, in particular by making them available in a structured, open and documented format on data.gouv.fr.
3. **Develop the risk assessment tools** (cost-benefit studies, socio-economic studies, etc.) needed (in agreement with Theme 1 of the COP) to ensure that risk management recommendations are better taken into account.
4. **Develop interdisciplinary methodological tools** (in agreement with Theme 1 of the COP) 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 consolidate synergies with expert appraisals** (in agreement with Theme 1 of the COP), particularly to obtain data that will provide insights on the exposome, and develop research to forecast the risks of the future. This will be pursued through support for the National Research Programme for Environmental and Occupational Health (PNR EST) and its calls for projects.
6. **Strengthen European and international collaboration** (in agreement with Theme 4 of the COP) by participating in research consortia, reinforcing bilateral relations with our counterparts, and contributing to the work of European organisations such as EFSA, EEA[34] and ECHA[35], or international organisations such as the WHO[36], etc., according to a "One substance, one assessment" approach.
7. **Participate in the development of regulatory frameworks at national and European level** to make them more effective.

[34] EEA: European Environment Agency
[35] ECHA: European Chemicals Agency
[36] WHO: World Health Organization

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 European Union'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[37] and CLP[38] 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. The Agency will also be working on its new missions to assess substances contained in cosmetics and tattoo products under the European regulation on cosmetic products and the REACH Regulation, provide support for market surveillance, carry out studies on substances and products, and ensure vigilance.

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 to run for seven years, 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. In addition to the nearly 200 national risk assessment and research institutions, 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.

[37] REACH: European Union regulation adopted to better protect human health and the environment from the risks associated with chemicals

[38] CLP: Regulation (EC) No 1272/2008 of 16 December 2008 on classification, labelling and packaging of substances and mixtures.

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), occupational exposure limits (OELs), biological values and health guidance values for drinking water. 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 is taking part in preparatory discussions on the changes needed to consolidate the system for producing maximum health values (Vmax).

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

- **Per- and polyfluoroalkyl substances (PFASs)**: In a context marked by a European restriction on all uses of PFASs initiated in early 2023 and a national PFAS plan for 2023–2027 led by the Ministry of Ecological Transition, ANSES is involved in major work focusing on PFAS monitoring. This concerns all environmental media and includes, in particular, an assessment of contamination, a ranking of the PFASs to be monitored and the determination of reference values.
- **Endocrine disruptors (EDs)**: ANSES, which is committed to the National Endocrine Disruptor Strategy (SNPE 2, currently at the end of its term), is continuing to assess substances with ED potential in order to present them at European level under the REACH and CLP Regulations, the latter of which has just introduced new hazard classes for EDs. 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 2024 will aim to identify the ones that really are a public health concern (for example, those that are of little use while posing a significant risk). In connection with Action 13 of the 4th National Health and Environment Plan (PNSE4), this work should help improve knowledge of the nanomaterials deployed in France, through a description of the industrial sectors that use them, and of the resulting exposure, based mainly on the analysis of data from the R-nano register that the Agency will continue to manage.
- **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:** Today, 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, in keeping with the priorities announced by all the Member States and the European Commission. ANSES will also be active in the assessment of applications for national and EU MAs for biocidal products. To this end, the Agency actively participates in the methodological development work 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 about consumer safety have arisen in previous risk assessments concerning exposure to **consumer products**. This has prompted the Agency to pursue its action in this field. 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, in order to improve the clarity of 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 diversity of devices and user practices, the variability of the emissions formed and the incomplete documentation on the hazards associated with inhalation of the ingredients and additives they contain. The Agency will produce an assessment of the risks of using tobacco-related products, in particular vaping products, and will pursue its scientific and technical support work at the request of the authorities, as part of the implementation of the national tobacco control programme and the revision of the aforementioned Tobacco Directive. As such, ANSES is involved in European work seeking to harmonise Member States' practices in tobacco product regulation (the second European Joint Action on Tobacco Control – JATC 2).

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 (DGS) in drawing up the texts that transpose it into French law.

The new provisions introduced by this Directive relate in particular to the assessment of materials in contact with water. The Agency is closely involved in work to harmonise assessments of materials compliance, led by the European Commission and ECHA since mid-2023.

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, their metabolites and PFASs 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. In 2024, an expert appraisal will be launched to assess the health risks associated with the impact of drought, exacerbated by climate change, on swimming pool operating procedures (e.g. emptying) and water quality.

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, grey water, rainwater, etc.), on which the Agency provides support with regulation. The Agency is also focusing on the potential consequences of climate change on water resources by identifying and ranking the associated health risks.

Lastly, ANSES will work to ramp up activity relating to its new mandate as national reference laboratory for the monitoring of SARS-CoV-2 in wastewater.

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, which is in line with the "zero pollution" ambition of the European Green Deal. ANSES will also continue its work on the health consequences of pollution phenomena such as sand haze and large-scale fires linked to climate change.

Regarding indoor air, the issues at stake are the assessment of risks associated with all the specific vectors of exposure in a broader view taking account of exposure in indoor environments: chemical, biological and physical agents – including temperature – and multi-source exposure that comes under the concept of the exposome. To this end, the Indoor Air Quality Observatory (OQAI) will be extended to include indoor environments more generally (OQEI), and will be run jointly by ANSES and the Scientific and Technical Centre for Building (CSTB).

Physical agents: heat, technological innovations and noise

The Agency will maintain its monitoring of 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) – a WHO agency – to collect data on population exposure to electromagnetic waves and health.

The use of digital tools and technologies, from a very early age, can have an impact on physical and mental health, especially by modifying behaviour. In 2024, the Agency will continue the expert appraisals already initiated to assess the effects – and their determinants – of the use of social media on the physical and mental health of adolescents.

Regarding noise pollution, the social cost of which is considerable in France, the Agency will continue to monitor changes in sources and modes of exposure to noise. 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, according to a One Health approach.

In a context where the impact of climate change is being taken into account, ANSES will be working to improve understanding of the health effects that could potentially arise in the event of extreme heat. The Agency will be examining the possibility of establishing health thresholds above which heat may have effects on health.

The multi-domain 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.).

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.).

Adapting surveillance systems to changes in epidemiological situations and methods, such as monitoring diseases using studies carried out on the vectors themselves, is also a major challenge.

Occupational health

Background

In 2024, the strategic orientations will be set in the context of implementation of the new Goals and performance contract (COP, 2023–2027), the third year of implementation of the Fourth Occupational Health Plan, and fundamental environmental and societal transformation (climate change, an ageing population, transformation of work and how it is organised, changes in technology and consumption patterns, etc.). These transformations will inevitably have (and are already having) repercussions on occupational health.

As a public agency committed to global health, ANSES has a duty to consider the impact of climate change as one of its top priorities. While the Agency's operations must contribute to the general reduction of carbon emissions, its missions place it at the forefront of assessing the health consequences of this change for humans, animals and plants. In fact, it had already begun to contribute to this when it published a pioneering report in 2018 on the health risks to workers associated with climate change. Armed with this experience, ANSES will continue – as a common thread running through all its occupational health expert appraisals – helping to identify the variations in exposure and risks in the workplace caused by climate change, and also to identify ways of mitigating and adapting to these changes in relation to work activities.

The second common thread that ANSES intends to consolidate in its occupational health expert appraisals concerns the subject of women's health in the workplace, a major and priority public health issue. With a view to increasing gender equality in companies, it is important to identify inequalities and differences between the situations of women and men, as well as their causes and specific characteristics. It is therefore necessary to gain a better understanding of women's working conditions and their potential health impact, as this is an essential prerequisite for deploying effective preventive measures that will benefit everyone, both within companies and in society as a whole.

Challenges

Improve anticipation of emerging occupational risks in the workplace

The detection of emerging or re-emerging occupational health risks is one of the Agency's fundamental missions. It relies on monitoring, research and vigilance work, in particular by the RNV3P's[39] WG on Emerging issues, which aims to detect emerging occupational diseases or new high-risk occupational situations. Thus, while pursuing its work to produce data and knowledge in support of research and expert appraisals, or for developing and harmonising the occupational exposure thesaurus, the Agency will endeavour, in accordance with Goal 2.1 of the COP[40], to continue strengthening and consolidating occupational health vigilance schemes and fostering links between the various health schemes to enable better detection of emerging risks in the workplace. This work will help meet Action 7.2 "Focus research on priority topics to ensure its relevance and operational nature, and on emerging risks" of the fourth Occupational Health Plan (PST4).

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. Much of this work concerns chemicals and is also related to implementation of French public policy actions (PST4, PNSE4, SNPE2, etc.) or the contribution to the implementation of European or national regulations on the assessment and management of chemical risks.

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

ANSES will also continue to provide a high level of support for the implementation of European regulations (CLP, REACH, Plant Protection Products, Biocides, Veterinary Medicinal Products), which include a component on occupational exposure and risks, thus contributing to the deployment of Theme 4 of the COP for a strong presence of the Agency regarding issues of expert appraisal at national, European and international level.

[39] National Network for the Monitoring and Prevention of Occupational Diseases
[40] Goal 2.1 of the COP: "Better anticipation of emerging threats"

From 2024, the Agency will also be responsible for the new activity of cosmetovigilance and assessment of cosmetics and tattoo products. As with all the above-mentioned regulations on chemical products, the assessment of cosmetics and tattoo products must take account of the exposure of end-users, including not only consumers but also the professionals applying these products.

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, most of which fall within the Agency's sphere of competence. The Agency will also continue to be involved in EU discussions on updating chemical regulations, to enable them to be improved on the basis of its experience with implementation.

Particular attention will also be paid to EDs[41], CMR[42] substances and respiratory sensitisers, as well as to "emerging" substances such as nanomaterials, which all require particular research, assessment and expert appraisal efforts, given the lack of knowledge about the effects associated with their specific properties and the risks they could pose in the workplace.

Once again, the major challenge for the Agency in 2024 and the years ahead will be to maintain the efforts already under way to develop and improve assessment methods that can take the combined effects of chemical mixtures into account and, beyond chemical risks, can take better account of the risks associated with multiple exposure. More broadly, the Agency will strengthen its ability to work in a multidisciplinary way and mobilise its wide range of skills in numerous areas in order to apply the concept of the exposome to its expert appraisals, continuing the implementation of the action plan resulting from its Scientific Board's opinion and report in 2022. The work being carried out under the PARC programme will provide some answers to these issues.

Lastly, the aim is also to better capitalise on the expert appraisals conducted within these different frameworks via the PST4 actions in order to improve risk awareness, information, occupational risk prevention and health protection in the workplace.

[41] EDs: Endocrine disruptors

[42] CMR: chemical agents which have carcinogenic, mutagenic or reprotoxic effects in the medium or long term

Maintain strong involvement in the investigation of multiple exposure situations 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. The Agency intends to maintain its momentum in this area, given the reality of workers' exposure in France[43]. In this approach, multiple exposure and the assessment of combined risks is a central and recurring issue. 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. Since the health crisis linked to COVID-19 and the significant rise in teleworking, these issues have become increasingly important for society as a whole, and call for the problems associated with new forms of work organisation to be anticipated in research and risk assessment work.

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 2024, several expert groups will be continuing or finalising their work, which focuses "in practice" on occupational settings involving multiple exposure.

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

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 continue 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 routinely during the Agency's ongoing expert appraisals on this key issue.

[43] See the ANSES-*Santé Publique France*-DARES study, which revealed that "almost all (97%) of the 25 million public- and private-sector employees experience conditions of multiple exposure", https://www.anses.fr/en/content/cumulatiexposure-workplace-12-profiles-inform-prevention-policies

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

Assessing risks 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 exposure assessment, 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 means of preventing or reducing them.

These competencies will now be deployed by a specific expert appraisal body – the Expert Committee on socio-economic analysis – which was set up in 2021. In line with Theme 1 of the COP, the aim will be to strengthen this mobilisation of socio-economic expertise for future work in occupational health, wherever it is possible and useful.

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, and guide the decisions of public authorities.

Under the National Research Programme for Environmental and Occupational Health (PNR EST), the Agency will continue giving 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.). In accordance with the goals of Theme 1 of the COP, the Agency will work to consolidate the PNR EST, which is the only programme that draws directly on expert appraisal recommendations to support public policy-making. This will involve seeking new funding and strengthening the links between ANSES and its research funding partners and stakeholders (the French Research Agency, ANR, in particular), in line with the national portal for calls for research projects and while preserving the specific nature of the questions to scientific teams arising from health and safety issues, particularly occupational health issues. This

objective should benefit from the discussions currently being led by ANSES as part of Goal 7 of the PST4 on developing research and improving knowledge, particularly on emerging risks. In 2024, these discussions will culminate in the drafting of an occupational health research strategy, from identification of the teams to be mobilised through to identification of an agenda of priority areas for stakeholders in this field. They will be formalised in a white paper.

At European level, ANSES will focus on implementing the goals of Theme 4 of the COP to ensure a strong presence at national, European and international level for the Agency's activities, particularly its research activities. Its aim in the field of occupational health from 2024 will be to join the European Perosh[44] network, whose purpose is coordination and cooperation between partners on research and development initiatives in occupational health and safety.

In addition, ANSES's teams are involved in the implementation of European-funded research projects 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[45] in Germany and RIVM in the Netherlands, or in North America with NIOSH[46] in the United States and INSPQ[47] in Quebec, Canada. 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[48]) and international bodies such as the WHO, particularly its Chemical Risk Assessment Network, or the International Agency for Research on Cancer (IARC), should be continued.

[44] Partnership for European Research in Occupational Safety and Health
[45] BAuA: Bundesanstalt für Arbeitsschutz und Arbeitsmedizin
(German Federal Institute for Occupational Safety and Health)
[46] NIOSH: National Institute for Occupational Safety and Health
[47] INSPQ: Institut national de santé publique du Québec
[48] EU-OSHA: European Agency for Safety and Health at Work

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 developments in farming practices and crop management techniques.

At European level, 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 elements relating to the health, economic and societal contexts.

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[49] and the IPPC[50]), 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 alerts in combating the risks that emerge and spread between countries or continents.

Challenges

Health risk assessment and national monitoring for better anticipation and prevention

(COP Goals 1.1 "Development of new expert appraisal approaches: increase the clarity of research into assessment methods", 2.1 "Better anticipation of emerging threats" and 4.1 "A strong presence regarding issues of expert appraisal and research at European and international level")

Current European regulations emphasise prevention, and a growing number of plant health hazards also impact other living compartments, as considered in the One Health approach. In this regard, and related to environmental health in a context of climate change, because current changes to the climate are significantly altering the areas and conditions of prohibited pests' potential establishment in France, it is 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. Regarding the implementation of general surveillance with a view to anticipation, the focus will be on wood-boring insects, which will be categorised once they have been collected in generic traps at European Union entry points.

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 active role in the work of the epidemiological surveillance platform for plant

[49] EPPO: European and Mediterranean Plant Protection Organisation
[50] IPPC: International Plant Protection Convention

health run with the DGAL, INRAE, the FREDON[51] network, Acta[52], the Chambers of Agriculture and CIRAD, by jointly leading or participating in thematic working groups (*Xylella fastidiosa*, the bacterium responsible for huanglongbing – HLB, Panama disease in banana crops). 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 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

(COP Goals 2.2 "Supporting State services in managing health crises", 3.1 "ANSES, a major player in research and analytical reference according to a One Health approach", 3.2 "Greater visibility and promotion of our research activity" and 4.1 "A strong presence regarding issues of expert appraisal and research at European and international level")

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, thousand cankers disease, citrus whitefly). 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.

[51] FREDON: national network tasked with monitoring France's botanical heritage, and managing species harmful to the health of humans, plants and the environment
[52] ACTA: Association for the coordination of agricultural methods, representing agricultural technical institutes and applied research organisations for animal and crop production

Continual improvement in the assessment of plant inputs...

(COP Goal 1.1 "Development of new expert appraisal approaches: increase the clarity of research into assessment methods")

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.

Efforts will continue to improve the efficiency observed in 2022–2023, by looking for ways to optimise assessment and decision-making processes to help achieve suitable examination times for applicant dossiers, particularly regarding plant protection products.

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.

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

(Goal 5.3 "Optimise the processing of formal requests and marketing authorisation (MA) applications")

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 and enables submission of the full technical dossier on this platform. 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. It will be extended to include certain active substances that are not candidates for substitution, as part of a joint response to a formal request, with INRAE.

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

(COP Goal 1.2 "Decisive action to advance the knowledge needed to assess health risks")

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 judicious 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 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 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 when it wishes 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 2024 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.

3. Summary of the work programmes of the scientific Divisions

Research and Reference Division

Introduction

ANSES's Research and Reference Division brings together the Agency's nine 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 28 international mandates were held by these laboratories in September 2023) 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. These laboratories also contribute to the **expert activities** carried out by the Agency in all these areas.

In line with the orientation letters for the laboratories and their units, which are drawn up every five years, and with ANSES's Goals and Performance Contract (COP), 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. The work sheets 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, were therefore presented to the supervisory ministries in autumn 2022 for the period 2023–2024. Their mid-term update was 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 2024 contained in these sheets, organised mainly according to the six transversal strategic axes 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 axes, 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 respective spheres of competence.

Cross-cutting projects led by the Strategy & Programmes Department

The DSP is responsible for supervising development 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 tasked with contributing to the implementation of this strategy through the coordination and facilitation 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 the work is carried out.

Efficiency

The process led by the DSP to **harmonise and consolidate the reference activities of the Agency's laboratories, with a view to improving efficiency**, will be pursued in 2024. As part of this, the in-house working group tasked with proposing guidelines and tools to bring about convergence in **diagnostic reagent verification practices** will continue its work, mainly on batch control by the national reference laboratories (NRLs). In 2024, the in-house group set up in late 2022 will continue work on harmonising practices for **calculating and using measurement uncertainty**. A **meeting of all the ANSES reference laboratories** will again be organised in the coming year to maintain momentum in exchanging practices and experience between laboratories responsible for reference activities at national (NRL) and European (EURL/EURC) levels, along with a **seminar for inter-laboratory proficiency test (ILPT) coordinators**, to continue to facilitate sharing and the search for common solutions in work in this area.

In the field of **biosafety**, the internal committee for the control of biological risks in laboratories, re-established in early 2023 and led by the DSP, will continue inter-laboratory coordination efforts in order to promote exchanges of experience, harmonisation of practices and development of shared tools to benefit all the laboratories. The DSP will also continue 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 analysing environmental samples and, more generally, during 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, with regard to the expected support for the health authorities during the **Paris 2024 Olympic and Paralympic Games**, the DSP, together with the Health Alerts & Vigilance Department (DAVS), will step up coordination of the various Agency entities that may be mobilised (in particular the laboratories), through their joint leadership of the dedicated in-house task force.

Major sector-specific projects

The coming year will again see our teams mobilised to implement the action plan following the **collective assessment 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 assessment. In particular, the following actions should be emphasised, in line with the objectives set in ANSES's new **Goals and Performance Contract (COP) for 2023–2027**:

- work to consolidate our policy on **biological assets**, by clarifying and disseminating our policy on external valorisation in this area;
- discussions and work aimed at structuring the policy and implementation procedures for **managing and exploiting laboratory data,** with the help of the relevant support and cross-functional departments and in consultation with the Agency's other core divisions.

Scientific coordination for each of the six transversal strategic axes (animal health & welfare, plant health, food safety, antimicrobial resistance, epidemiology & surveillance, exposure to and toxicity of chemical contaminants) promoted by the six scientific directors will continue in 2024. 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.). Based on the recommendations of the collective assessment, inter-axis coordination will be proposed to strengthen integrative coordination. In particular, emphasis will be placed on integrating the challenges of climate change and its health impacts into the Agency's scientific orientations and activities.

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 the call for expressions of interest issued in late 2023 will begin in 2024. The aim is still to fund exploratory projects in line with the strategic research and reference priorities, particularly by breaking down barriers and fostering closer scientific ties between the different ANSES teams, as well as in terms of collaborative strength with key external partners with whom the Agency has signed framework agreements, or with regard to its response to questions from risk assessors, to the potential for indusrial application, to the mobilising of participatory research, etc.

In 2024, the DSP will once 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 other French research institutes and schools (INRAE, CIRAD, VetAgro Sup, the CEA, Oniris and Ifremer).

Lastly, in 2024, the DSP will once more 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 information exchanges 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 2024 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 reference and surveillance activities. This will enable the Agency to carry out its diagnosis and surveillance activities more quickly, efficiently and with greater robustness, in order to safeguard public health, in line with the objectives for food-chain surveillance set out in the 2023–2027 COP.

In 2024, 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/or 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 tools that safeguard health, 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 Companies for technology transfer acceleration (SATT), 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 at national level

The DSP will continue to support the laboratories in **developing scientific and institutional partnerships** in an ever-changing context, in line with the orientations set out in the 2023–2027 COP. The DSP will oversee effective implementation of the framework partnership agreements signed with various French research and technical organisations (INRAE, CIRAD, Ifremer, ACTA, ACTIA, CEA, etc.) and propose new structural partnerships. In particular, it will continue to develop partnerships with players in the human public health sector (working with the *Institut Pasteur* to draft a possible framework agreement) and the environmental health sector (mainly the French Biodiversity Agency - OFB).

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 university groupings (COMUE) and our laboratories' standing with the Regional Councils.

The process of **strengthening synergies between NRLs and their public health counterparts (the National reference centres - NRCs)** will be pursued in conjunction with *Santé Publique France*, with the aim of further improving mutual knowledge and understanding, which is the basis for deeper 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 2024 to the forging of **European research partnerships for Horizon Europe**[53]. These are markedly shaping the European research landscape in our fields of activity.

The DSP and the DAEI will remain 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 continue its central involvement in preparing and implementing the **Partnership on animal health and welfare (PAHW)**, as well as in the proposed partnership on food safety according to a One Health approach, following on from the work of the One Health European Joint Programme (EJP), which comes to an end in late 2023. The DSP will also continue to closely monitor the establishment of other partnerships of interest (especially those relating to food systems and antimicrobial resistance as part of a One Health approach, and pandemic preparedness).

Lastly, 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 dedicated scientific and technical resources from the Ploufragan-Plouzané-Niort Laboratory and several European partners.

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

Laboratory activities for the animal health and welfare axis

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 controlling animal and zoonotic diseases and, where necessary, managing health crises. It enables ANSES to apply a comprehensive and systemic approach to issues of research and assessment in animal health and welfare, taking account of different farming systems and their consequences on animals, on the health of animal production professionals 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. Global changes and their impact on the factors of pathogen emergence, development or persistence are also leading ANSES's research teams to broaden their activities to cover new hazards or challenges. 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 being transmitted to certain animals, avian influenza viruses adapting to mammals, the emergence of indigenous human cases of West Nile fever and the arrival of epizootic haemorrhagic disease on the European continent – that 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 areas converge.

The ANSES laboratories' 2024 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 cell ultrastructure level;
- **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 2024 implementation of these major strategic themes are highlighted here.

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

- In 2024, the ANSES laboratories with national and European reference mandates will continue adapting their activities to the new regulatory context. This concerns new regulated animal diseases (Surra, porcine reproductive and respiratory syndrome - PRRS) and new animal species now 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 proficiency 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 on top of the classic national and European analytical reference missions.
- 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, through their proficiency in the related tools

and their active monitoring of methodological developments, mainly for high-throughput sequencing using **new third-generation sequencing techniques**. This know-how enables these technologies to be deployed in the laboratories: **MinION** (e.g. African horse sickness, foot-and-mouth disease, West Nile, epizootic haemorrhagic disease), **digital PCR** (analysis of complex matrices – with inhibition phenomena, useful for determining germ viability, etc.), **aptamer**-based technology (various parasites such as *Trichinella,* etc.), with several ultimate objectives including new screening/diagnostic tools and the prospect of therapeutic tools offering an alternative to antibiotics/antiparasitics. Early detection requires techniques that can be used on-site for sick livestock animals, and these are being explored in several work programme projects (LAMP for nematodes, for avian influenza, etc.). **Serology techniques** will also need to be developed for certain diseases (e.g. serology for Venezuelan encephalitis) or evolve to better characterise immune responses (sequencing of **antibody repertoires** in pigs applied to porcine respiratory complex and pestiviruses).

- 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.) require proficiency in sequencing and analysis of results, but also, prior to this, analysis of the reliability of the phylodynamics methods themselves (epidemiology work).
- **Innovation** also means continually adding **new matrices to which the current analysis methods must be adapted, and developing new tools**. Whether it concerns improving early detection of an infection, including by adapting to sampling in the farm environment (highly pathogenic avian influenza), or studying pathogen transmission (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 methods tailored to multiple matrices represents one of the challenges for the work programme**.
- As well as for detecting the pathogens themselves, innovation in methods is also important for determining pathogen resistance to chemicals used for their control. For example, the International coordination of research on infectious animal diseases (ICRAD) project METABOL-AR will explore the application of metabolomics to detecting resistance to antiparasitic drugs in gastointestinal nematodes.
- The reference laboratories will also be committed to **helping reorganise diagnosis 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. Similarly, the updating of certain infectious disease control plans will require the close involvement of the corresponding reference laboratories (e.g. paratuberculosis).

- Lastly, the **numerous European and international reference mandates in animal health and welfare** held by the ANSES laboratories give them a very broad view of infectious animal diseases and provide them with invaluable data for **international monitoring** of these diseases. The laboratories therefore devote part of their work programme to building lasting expertise that is recognised at European and international level, for example in the monitoring of foot-and-mouth disease, bluetongue serotypes, epizootic haemorrhagic disease virus, melioidosis, rabies, etc.

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 move 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** or between **the RNA of pathogens and the cellular proteins of their hosts** are central to several ongoing and future laboratory projects. These include the finalisation of PersIstOmics and PersIFA on foot-and-mouth disease, IPPA on high-throughput mapping of host-virus interactions in African swine fever, LAGMED on rabbit viral haemorrhagic disease virus, and a comparative study of the interactomes of ORF3 and related proteins in porcine coronaviruses.

This is also the case with studies on flaviviruses (West Nile) within the framework of the Laboratory of excellence in integrative biology of infectious diseases (LabEx IBEID), and the TrichinEV project, which seeks to characterise the extracellular vesicles produced by the zoonotic parasite *Trichinella* but also by the host's muscle cells in response to cell invasion, among others.

- The effect of climate change on virus-host interactions is also on the work programme (e.g. Aquaterm and Gourhannic projects on fish diseases).
- 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), or to model the molecular protein-protein and RNA-protein dialogue between viruses and ticks using Hazara and Dugbé viruses as models of Crimean-Congo (in the MOSATICC project).

- Lastly, some novel projects are now focusing on the interactions between pathogens and the "host or vector + its microbiota" entity, also known as the "**holobiont**", in order to determine the impact of these microbiota on the response of the host or vector to the infectious agent.

These different approaches (ultrastructural, -omic, cellular, etc.) are now seen as essential tools, used 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), but also to strengthen disease control methods by providing knowledge of host-virus interactions coupled with epidemiological modelling work (enzootic bovine leucosis).

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**, **tuberculosis** and **animal botulism**. These projects call on a variety of approaches, whether epidemiological, analysis of favourable environmental conditions, or the study of **interactions between infectious agents and environmental amoebae**.

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 the raccoon (an invasive alien mammal in Europe), work to map the risk of tick-borne encephalitis virus (TBEV) in France, and several European projects on bats and rodents, related to emerging risks.

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 2024. Having passed a decisive milestone in development of the ASFV-989 candidate vaccine against **ASF**, work will continue as part of a maturation project supported by SATT Ouest Valorisation, the technology transfer accelerator, in which ANSES will continue development (vaccine challenges, reversion safety, etc.) at its facilities, with a view to moving towards the industrial transfer of a vaccine. 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 test 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. Lastly, new control methods are also being sought in the **area of parasitic infestations**. A project on chicken nematodes (ANTINEMA) will seek to test a new vaccine for the long-term control of *Ascaridia* and *Heterakis* infections in poultry, if it is selected for funding under the ERA-NET ICRAD call for projects.

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 continue managing a project to **vaccinate badgers against bovine tuberculosis** in the Dordogne *département*.

It should be noted that as part of the support in combating health crises provided by the NRLs to the authorities, a **programme to vaccinate poultry against avian influenza** will be rolled out across the country during 2023–2024, and will be accompanied by significant analytical activity coordinated by the NRL to monitor this vaccination.

- **Other antiviral strategies** are being investigated in addition to vaccination. Several projects in the work programme focus on research and assessment of **antiviral substances** against various pathogens, such as viral infections of the human and equine central nervous systems (flaviviruses such as tick-borne encephalitis virus, West Nile disease and alphaviruses responsible for equine encephalitis). Moreover, as part of the creation of the GenHomEqui contracted unit with Inserm's DYNAMICURE unit, for developing One Health translational

research in animal health (horses) and human health, 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.

- 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 **HARIZONA** 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, while taking account of the impact of climate change. Moreover, the 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. Lastly, a new group set up within a research team will focus on the search for a new strategy to combat resistance to anthelmintics, based on the detection of new targets, mainly G protein-coupled receptors (GPCRs), but also by targeting the viruses found in these parasites.

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 (ex. the **PIGAL** project: "Alternative **pig farming**: opportunities and risks associated with animal health, welfare and biosecurity")

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. This is also true for the **Netpoulsafe** and **BroilerNet** projects, which are bringing together European poultry sector players in order to improve compliance with biosecurity measures and suggest innovations for sustainable production, while taking animal welfare into account.

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

- 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 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 will carry out work on identifying poultry depopulation methods during epidemics.

In terms of reference activities, ANSES also contributes its expertise to the work of the National reference centre (NRC) 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.

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, porcine intestinal organoids for the study of host-pathogen interactions during porcine enteric viral diseases), 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' 2024 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. Some 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. Subject to funding, a project will begin in 2024 to study the impact of pesticides on the immune systems of bats and rodents and on the emergence or re-emergence of pathogenic micro-organisms.

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.

Pivotal European partnerships

Following the European Commission's acceptance in 2023 of the Partnership on animal health and welfare (PAHW) as part of the Horizon Europe programme, the Agency will work with its partners on its scientific and strategic implementation, as well as on planning the first calls for projects scheduled for late 2024–early 2025. This European partnership will be the keystone of European research and reference in animal health and welfare for the next decade.

Laboratory activities for the plant health axis

The increased frequency, volume and diversity of world trade in plant products, the impacts of global climate change, developments in farming practices and crop management techniques, changes in the range of insect vectors of disease, 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 and technical work on pests to plant health – including invasive plants – in cultivated, forest and natural environments. The LSV's scope also covers insect vectors, insects that are beneficial to plant health, detection and identification of genetically modified plants, and quarantine of plants introduced into France 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 work through its Epidemiology and Surveillance Support (EAS) Unit, mainly as part of the national epidemiological surveillance platform.

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

- involves studying pests' interactions 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 master and doctoral students, and post-doctoral researchers. 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 or management strategies in the field.

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 are 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 regulations now consider the French overseas *départements* and regions (DROM) to be third countries, specific corresponding regulations need to 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.

In this European regulatory framework, 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 environments 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 European Union Reference Laboratory (EURL) mandates in plant health, whose activities started in 2019. ANSES's three EURL mandates (plant-parasitic nematodes, insects and mites, fungi and oomycetes) will be included in the third biennial work programme, with the main objectives – besides the organisation of ILPTs and training courses for 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 previous work programme, three pests will continue to receive particular attention in the current French plant health landscape: the ***Xylella fastidiosa*** bacterium, the bacterium responsible for yellow dragon 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*. We will also continue to participate in maintaining the interface for consulting and visualising French surveillance data, and analysing these data (reports and maps). Regarding 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 ILPTs 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 ILPTs will be supplemented by the transmission and analysis of French data (see *X. fastidiosa* above). With lethal yellowing palm disease, for which several new outbreaks have 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 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 Directorate General for Food (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 (EFSA, EPPO or IPPC panels and working groups, other EURLs).

Standards, technologies and methodologies that guarantee innovation and quality

With the requirements of the 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 under the aegis of the Strategy & Programmes Department, 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 GMO 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, which has been renewed for another four years, an innovative methodology for monitoring the media and scientific literature will continue to be deployed with a view to early identification of new emerging or re-emerging pests within the EU, to meet the requirements of the regulations.

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

Not only will 2024 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. In addition to the link 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, there is the **CASPER USC** (with INRAE's SPE Department), the **NemAlliance cluster** (INRAE Brittany-Normandy Centre) for the study of plant-parasitic nematodes, the **Mycology contracted unit** (INRAE's Ecology & Biodiversity Department) for the study of fungi and oomycetes affecting forest tree species, and the **DIAGEPITROP partnership via a research agreement** for our unit based on Reunion Island (CIRAD) regarding emerging pathogen and pest populations for the French overseas territories and the South-West Indian Ocean/Southern Africa/East Africa region. We will also begin setting up **associate partner laboratory** status with INRAE for the Entomology and Botany 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.

ANSES will continue its involvement in the working groups of the **national epidemiological surveillance platform for plant health**, in both its thematic groups (mainly those dedicated to *Xylella fastidiosa,* HLB, Foc TR4) and those focusing on methodological work (international health monitoring, health reports, data quality, etc.).

In addition, our contribution to surveillance will now become further entrenched through the provision of our data to the platform as needed and scientific support in analytical fields.

The Agency will also be involved in monitoring emerging resistance to PPPs within the framework of the "Unintended effects and Resistance" component of the DGAL's biological surveillance of France (SBT) scheme, 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 constitutes 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.

Laboratory activities for the food safety axis

Food safety is a major and historical area for the Agency, and interacts strongly with four other transversal axes (animal health, antimicrobial resistance, exposure-toxicology, epidemiology-surveillance). The laboratory activities carried out under this axis 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 monitoring programmes for chemical and biological contaminants potentially found in food and water, and affecting public health. 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, surveillance, research and expert appraisal activities on a vast number of chemical, biological and microbiological contaminants that may be responsible for adverse effects, infection and/or food poisoning in humans. The information presented below will focus on microbiological hazards, while information on chemical hazards of natural or anthropogenic origin is detailed in this document under the "Exposure to and toxicology of chemical contaminants" axis.

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 in 2024, particularly for reinforced surveillance plans and health alerts in connection with the Paris Olympic and Paralympic Games.

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 2024, therefore, the laboratories will be able to implement complementary analytical methods for monitoring and control plans or official controls for *Listeria*, *Salmonella*, *Campylobacter,* enterotoxin-producing *Staphylococcus aureus*, *Clostridium botulinum*, *Bacillus cereus*, *Cronobacter*, hepatitis A virus, norovirus, histamine, biogenic amines and marine biotoxins. As part of the monitoring of these pathogens, the laboratories will carry out whole genome sequencing on a selection of isolates proposed and validated with the DGAL. Some analyses will also be conducted under the Marine Strategy Framework Directive (MSFD), the third total diet study (TDS3), 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 be exploited to support **work related to risk assessment**, refine work on **source attribution**, and contribute to the **investigation of microbiological contamination from farm to fork**.

The food safety research carried out by the Agency's laboratories 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, OE-VTEC thesis on *E. coli* in aquatic environments, Evanhoty project on *Yersinia* in pig and cattle production, "Into the waste" project on the hygiene quality of compost, Chaboté thesis on botulism in ponds, PaperFish and Animode projects 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, Salmo-Bond project on *Salmonella* adaptation factors in pig and dairy environments, Physallis thesis on the physiological state of *Listeria monocytogenes*, TBEV cross-cutting project on 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, Maresistome project 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 and Baclait projects 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). 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 and Interaclim thesis 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 to measure the health impact of bioinsecticides based on *B. thuringiensis*) and for defining **innovative approaches for the control** of zoonotic pathogens (Rezolve, Sanimetha and Bter projects).

Technological and methodological innovations for the detection of emerging hazards

The recent organisation of whole genome sequencing (WGS) activities 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 2024 as part of reference and monitoring activities on microbiological contaminants, following the agreement reached 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 Laboratory for Food Safety (LSAl) and the Laboratory for Animal Health (LSAn), 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, OMEVIB thesis). More generally, "-omic" 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).

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 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; 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 National reference centres in human health (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 continue within projects such as PROTOX (approaches for testing the *in vitro* toxicity of new proteins) and RIMICIA (microbiomes of the human and animal gastrointestinal tract). In addition, EFSA is progressively setting up a scheme to enable Member States to transmit and compare genomic data from WGS of foodborne pathogenic bacteria, in conjunction with the European Centre for Disease Prevention and Control (ECDC). ANSES is closely involved in this European **One Health Molecular Typing System** structure for surveillance and investigation of the targeted pathogens (initially *Listeria monocytogenes*, *Salmonella* and STEC),

including through its EURL on *Lm,* even more so since ANSES's 2022 appointment as the national coordinator for data transmission and for laboratories providing data (transmission mobilising the NRLs for *Salmonella* and *Listeria*).

These European collaborations are continuing 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 under way, and include the FOREWARN project on the occurrence, fate and behaviour of emerging pathogens in coastal surface waters within the framework of the Aquatic Pollutants programme, the HOLiFOOD project for a holistic approach to tackling food system risks in a changing global environment, and the Catalyse project on creation of a network of food safety players bringing together public and private partners to control microbiological hazards.

Laboratory activities for the antimicrobial resistance axis

Antimicrobial resistance is a major public health problem with a wide-ranging impact, involving issues of human and animal treatment, but also threatening our ecosystems. In the animal sector, the two EcoAntibio plans deployed since 2012 (2012–2016 and 2017–2022) have achieved very significant numerical objectives in reducing animal exposure to antibiotics and the prevalence of resistant bacteria in these populations. The third EcoAntibio plan launched in 2023 will enable current efforts to continue, including a cross-sectoral contribution structured by the renewal, also in 2023, of the Interministerial Roadmap (FIM) to combat antimicrobial resistance. ANSES's "Antimicrobial resistance" transversal strategic axis aims to coordinate and promote synergies in the Agency's various skills on this issue, in order to provide the public authorities with support and scientific expertise in line with 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

Implementation of **regulatory analyses within the framework of the NRL's activities** has been stepped up since 2021, 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 among the bacteria *Campylobacter* spp., *Escherichia coli* and *Salmonella* in animals on arrival at the slaughterhouse (caeca) and during distribution (retail meat). Having been 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[54] network and the Vigimyc[55] network for mycoplasmas). With regard to the Resapath network, structural changes have been 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 was used to model Resapath data in order to characterise changes in the susceptibility of *Escherichia coli* clinical isolates to colistin (COBAYE Project, EcoAntibio). In 2024, 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 done at European level by EFSA, the EMA and the ECDC (JIACRA or Joint Interagency Antimicrobial Consumption and Resistance Analysis).

In 2024, 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 hospital settings, antimicrobial resistance of mycoplasmas), mainly with the last remaining research funding from the EcoAntibio 2 plan. 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 this context, ANSES will continue contributing to implementation of One Health monitoring of antimicrobial resistance, particularly during resumption of work for the FIM and the EcoAntibio 3 plan in 2024.

At European level, in the framework of the **EU-JAMRAI** European 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 2024 and beyond. In 2022, the French Presidency of the Council of the European Union (FPEU) reaffirmed the importance of the EARS-Vet scheme, which is now funded by Europe's EU4Health programme, and the work has been included on the agenda of the next joint action (**EU-JAMRAI 2**) from the end of 2023, for a period of four years.

[54] Surveillance network for antimicrobial resistance in pathogenic bacteria isolated from farm and companion animals in France

[55] Monitoring network of pathogenic mycoplasmas in ruminants

Pursuing methodological developments for the detection of antimicrobial resistance

In 2024, 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 in 2024.

Better characterisation of the resistome and antimicrobial resistance gene flows

In 2024, 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. Projects funded under the latter either came to an end in 2023 or will be developed in 2024. This work will also be continued or finalised as part of European projects such as PRE-EMPT (One Health EJP), or projects funded or co-funded by ANSES (MASTOC and CARAVANE). 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 will also continue (for example, the ENVIRE project on chickens, which is 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, JPI-AMR). 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, research on the adaptation of bacterial biofilms to biocides and the consequences on antimicrobial resistance will continue in 2024 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), which was studied extensively until 2023 (RESPEC, CANIPHAGE, EVASION, EcoAntibio 2 projects), will continue in the context of the final EcoAntibio 2 call for 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 in disciplinary fields other than those usually covered. Following the same approach as for the work on the formal request on the risks associated with antimicrobial resistance in environmental media initiated in 2018 by the Risk Assessment Department (DER), 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 was finalised in 2023. More generally, all the interface work carried out over the last few years between laboratories and assessment departments (particularly the DER and ANMV) provided input in 2023 for the debates on the drafting of the EcoAntibio 3 plan, within the framework of the FIM that was also renewed. Lastly, 2024 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 2024, 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 2023 to conduct an inter-laboratory test on antimicrobial resistance in African countries, similar to what is done in the Resapath network, and as a pilot project that may possibly be resumed in 2024 with FAO funding. 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 2024 as part of this mandate, as well as in collaboration with the ENSV-FVI veterinary school (part of VetAgro Sup), and will include sociological aspects. ANSES's partnership with the Mérieux Foundation further strengthens this international positioning on antimicrobial resistance.

Laboratory activities for the epidemiology and surveillance axis

The ANSES units working in epidemiology:

- provide scientific and technical support to ANSES's supervisory ministries, partner organisations and risk assessment departments, in particular on Category ADE/BDE 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 steering committees, working groups and depending on the case, coordination teams and operational teams;
- make a significant contribution to the production of articles for the *Bulletin Epidémiologique* on Animal Health & Food Safety 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 addition to surveillance, which is an ongoing activity, the epidemiologists at ANSES study the spread of zoonotic diseases/agents and other hazards in populations and ecosystems. This work is designed to both predict their spread and measure the impact of management measures.

In 2024, they will again offer major scientific and technical support and carry out key research on Category ADE/BDE animal diseases, in particular avian influenza, but also tuberculosis and brucellosis. In addition to this vital groundwork, ANSES's other key epidemiological work for 2024 will focus on studying the importance of wildlife as a reservoir for certain diseases, epidemiology of antimicrobial resistance, and methodological innovation.

Epidemiology of avian influenza

On the issue of highly pathogenic avian influenza (HPAI), which is still very topical, the use of models of disease spread 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. Analytical epidemiology work will also be carried out on the recurrence, persistence and spread of HPAI viruses (including in vaccinated situations). The

emergence of zoonotic HPAI viruses will be analysed at the interface between wildlife, domestic animals and humans, taking molecular, ecological, social, environmental and epidemiological factors into account.

Epidemiology of tuberculosis and brucellosis

Tuberculosis and brucellosis are two Category BDE animal diseases for certain species that are closely monitored and studied.

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

- indicators and risk factors for *Mycobacterium bovis* infection in badgers and wild boar in the enzootic area;
- monitoring vaccination of badgers by injection as a complementary measure for controlling bovine tuberculosis in an enzootic area in Dordogne.

Research will also be conducted on brucellosis. A field survey will provide an estimate of the seroprevalence of *Brucella canis* infection on dog farms in France and be used to identify the risk factors for infection. Thesis work will also be completed on the transmission dynamics of bovine brucellosis in Paraguay and the assessment of monitoring and control strategies.

Role of the wildlife reservoir

The wildlife compartment plays a key role in the emergence, perpetuation and resurgence of many animal and/or human diseases, as illustrated in the previous paragraphs for avian influenza and tuberculosis. The coming year will be an opportunity to conduct or complete several epidemiological studies and investigations to update knowledge on different infections in wildlife.

With this in mind, infection of foxes by *Echinococcus multilocularis* will be quantified in the South-East France expansion zone, with a search for any intermediate hosts that could enable the parasite cycle to be maintained. Similarly, an analysis of the raccoon's role as a reservoir for *Baylisascaris procyonis* in Alsace, Lorraine and Auvergne will be conducted.

Lastly, as part of a One Health approach, the risk of botulism in wild birds will be assessed.

Epidemiology of antimicrobial resistance

In the field of epidemiology of antimicrobial resistance, studies will continue on the dynamics of resistant bacteria and/or resistance genes between animal and human populations, using statistical and modelling approaches. A quantitative analysis of the risk of exposure to antimicrobial resistance

from different sources will be undertaken, as well as a study of the measures influencing the transmission dynamics of antimicrobial resistance from chicken farms to the environment. Phylodynamic approaches will be used to examine the spread of antibiotic-resistant clones or lines in pets and cattle.

Comparative analyses of data on use and resistance will also continue. An approach using dynamic panel models will enable an integrated One Health analysis of antimicrobial resistance surveillance data in Europe. These models are used to estimate the potentially delayed impact over time of the measures taken. Other work will assess the impact of reducing antibiotic use on resistance levels in cattle and domestic carnivores.

Methodological innovation

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 Nowcasting project will use very short-term analytical forecasting methods to better estimate the actual incidence of disease in affected areas. The results will help improve the accuracy of qualitative and quantitative assessments of the risk of disease introduction and/or spread. The impact of biases in the data on the results produced by phylodynamic models will also be studied, with application to bovine tuberculosis. Lastly, the use of deep learning approaches to detect health events and map risks (cattle mortality, West Nile) will be studied in greater depth.

Laboratory activities for the exposure to and toxicology of chemical contaminants axis

Exposure to chemicals and their impact on public health and the environment are major issues in the context of sustainable development. Implementing a sustainable chemicals strategy requires early identification of hazardous substances through continuous improvement of methods for assessing hazards, exposure and risks, as well as the implementation of rapid-alert systems based on monitoring and control. All these methods are constantly evolving to meet the challenges posed by the vast number of chemicals to which living beings are exposed, impacting human health (in our daily and professional lives), ecosystems and animal health. In coordinating the European Partnership for the Assessment of Risks from Chemicals (PARC), the Agency is leading a vast network of research institutes, public health agencies, environmental agencies and laboratories involved in monitoring. The "Exposure to and toxicology of chemical contaminants" strategic axis aims to promote synergies in the Agency's various skills in this field, based on a comprehensive One Health approach.

More specifically, the ANSES laboratories are contributing to this axis through:

- monitoring and control of residues of veterinary medicinal products, plant protection products, disinfectant biocides, trace metal elements and toxins (phyco-, bacterio- and biogenic amines) in foodstuffs of animal origin;
- monitoring and control of chemicals in water;
- development of analytical tools for monitoring microplastics;
- characterisation of hazards to the health of humans and animals (bees, fish);
- development of new methodological approaches;
- contribution to characterising exposure to several classes of substances as part of the third total diet study (TDS3), coordinated by the Agency (DER) and to the study of dietary exposure to chlordecone in the French Caribbean population;
- study of the fate of these substances in the environment, humans and animals.

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**) origin in food, hive products and water have been entrusted to the Agency's laboratories, which 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 implementation of Regulation (EU) 2021/808 is leading to a review of all analytical methods. New methods covering substances common to the two regulations on **plant protection products** and **veterinary medicinal products** will be validated

according to common principles. Methods for detecting residues of **banned antibiotics** using various biochemical tests will be assessed, and electrochemical methods will be developed and validated. For **marine biotoxins**, an effect-directed physico-chemical analysis method (Neuro-2A cell-based assay) will be introduced and the analysis spectrum will be extended to new taxa and toxin analogues. In water, national campaigns will focus on per- and polyfluoroalkyl substances (PFASs, including short-chain PFASs) and pesticides, which will contribute to TDS3. Analytical methods will continue to be developed for highly polar compounds, including pesticide metabolites, PFASs, speciation of arsenic, mercury and chromium (TDS3), disinfection by-products and cyanotoxins.

Non-targeted screening based on high-resolution spectrometry will be used for monitoring veterinary drug residues in foodstuffs and as part of a water monitoring campaign.

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**).

Technological and methodological innovations currently being integrated

As part of their cross-functional work and in connection with the European PARC partnership, the laboratories are continuing their cooperation on the use of **high-resolution mass spectrometry** for developing broad-spectrum analysis protocols with regard to the substances screened for (multiple classes), signal processing to screen for known (post-target analysis of suspect substances) or unknown (non-targeted analysis) substances, and the creation of virtual sample libraries. The units are also collaborating on effect-directed analytical approaches. These methods will be used in monitoring and control plans for veterinary drug residues and biotoxins, and in a dedicated water campaign. Biosensor-based tools will also be developed for detecting disinfectant biocides from the quaternary ammonium and chlorate classes in the agri-food industry.

Providing knowledge useful for characterising hazards and understanding the fate of chemical contaminants

To help characterise hazards for humans, several national and European research projects will be extrapolating absorption, distribution, metabolism and excretion processes from *in vitro* to *in vivo*. The toxic potential (cellular toxicity, genotoxicity, neurodegeneration, inflammatory diseases) of substances belonging to different classes (toxins, nanomaterials, microplastics, plastic additives, pesticides) will be characterised. Several of these projects will contribute to method harmonisation and validation, data sharing and the development of integrated testing and risk assessment methods. The effects of pesticides on neurodegenerative diseases, and of microplastics and quaternary ammonium on chronic inflammatory bowel diseases, will be studied using dedicated animal models.

In animal health, work will continue on the immunotoxicity of endocrine disruptors in fish, and on the impact of pesticides on bee mortality. The Agency is currently participating in the development of a platform incorporating kinetic and dynamic models for assessing chemical risks in animal species.

Lastly, the laboratories will take part in research into the contamination of various environments by chemicals (emerging pollutants, pesticides, PFASs, trace metal elements), and microplastics and their effects. They will also study their fate during food processing and cooking.

Science for Expertise Division

In line with the strategic orientations by thematic area on the one hand, and implementation **of the 2023–2027 goals and performance contract** (COP) – which has now been signed – 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, and with input from stakeholders. This summary sets out the teams' commitment to safeguarding health. Without being exhaustive, it gives some perspective to major actions that help increase the efficiency and scientific robustness of ANSES's work, advance major projects in the various specialist areas, prepare and support developments in response to health and societal challenges, enhance institutional communication on the Agency's role, challenges and utility, and integrate 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. Increasing the robustness of our work, using holistic approaches and improving efficiency

These challenges mainly correspond to two themes of the new COP: Theme 5, entitled "Transparent, efficiency-oriented action", which is largely supported by the division's work; and Theme 1, whose wording is resolutely geared towards **new, more holistic approaches** and developing the scope of the missions. Obviously, there is an ongoing imperative to **ensure the robustness of the expert appraisal processes**, a necessary condition for their credibility, and the Agency is working to strengthen this on the basis of its Scientific Board's recommendations.

In order to mobilise new expert appraisal approaches in the future, it is important to work today on research to develop and validate them. Besides its involvement in a broad portfolio of research activities, such as the European Partnership for the Assessment of Risks from Chemicals (PARC), for which the involvement of the Risk Assessment Department (DER) has been outlined (Sheet 5.7.2), **2024 will provide an opportunity to draft a chapter on "research into assessment methodologies" and include it** in the strategic orientations that guide the research work of the Agency's entities (milestone in Goal 1.1).

With regard to the integration of socio-economic analysis, using its different tools and disciplinary components, one of the work programme sheets of the Social Sciences, Economics & Society Department (DiSSES) (Sheet 7.1) lists the deliverables of the expert appraisals in progress, or due to

be launched in 2024. It contains no fewer than 18 expert appraisals, divided equally between formal requests (9) and internal requests (9) and covering all areas: food safety & nutrition (3), occupational health (6), plant health (2), animal health (3) and environmental health (4). A **roadmap (Sheet 7.3) has now been drawn up to guide the methodological work** to be carried out in socio-economic analysis, in response to the corresponding COP goal, in addition to the debate (Sheet 7.4) on the range of partnerships for developing study or research projects.

As an additional demonstration of a more holistic approach to risks, the expert appraisals that will apply the recommendations of the Exposome WG (Sheet 5.8.1) and **integrate "One Health" and "exposome" components into their expert appraisal approach, will be identified under the corresponding COP goal** (Theme 1.3). One example of this is the response to the internal request – with work now under way – on the cadmium cycle (Sheet 1.9.4), to conduct a detailed investigation of the determinants of exposure and compare them with the results of *Santé publique France's* Esteban internal contamination study, in order to identify possible levers for avoiding the upward trend in this exposure. This work also includes an socio-economic analysis component.

Teams from the division and beyond will be mobilised on another major programme, resulting from the ACCMER working group's efforts to **deploy the recommendations of the Agency's Scientific Board on taking the weight of evidence and uncertainty into account** (Sheet 5.8.2). After a longer-than-anticipated design phase, the support and testing phase is scheduled to take place over a three-year period, during which regular reviews will be carried out and possible adjustments made to implementation of the recommendations.

Regarding the **ranking of hazards and risks to food safety**, ANSES is continuing expert appraisal 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 work sheet (1.8.6). In 2024, work will mainly focus on the cattle sector (finalisation) and on plant sectors in connection with the **formal request on the risk rating for scheduling official controls in the field of foodstuffs of plant origin** (Sheet 1.3.11). This formal request is in line with the implementation of a single body to enforce health policy under the aegis of the DGAL.

In terms of the **efficiency and management of expert appraisals**, the COP goals are achieved through the contribution of opinions and reports finalised during the year, reflected in aggregate indicators. This is the case, for example, with meeting contractual deadlines for formal requests (indicators in § 5.3 of the COP). In 2024, particular attention will be paid to two specific points: firstly, the contract agreement period. Improving this also calls for more upstream information from sponsors **for scheduled work, and even more so for any unscheduled formal requests**. The second point is to inform the sponsors as early as possible when contractual deadlines cannot be met. A **close dialogue will be established** to identify the impact and possible solutions, particularly when the context imposes major time constraints on a response. With regard to emergency formal requests, the revised protocol will be implemented as soon as it has been validated. Another growing need for

sponsors is to obtain answers to questions covering a very broad field, exceeding the scope of ANSES's work. After devoting 2023 to identifying work of this nature, in 2024 the Agency will propose a draft generic protocol for cooperation, in accordance with the COP milestone in § 1.1.

With the same aim of optimising expert appraisals, and following the introduction of the new document-sharing platform (RESANA), which also enables the co-authoring of collective documents, the **focus in 2024 will be on the technical equipment in the meeting rooms** used for collective expert appraisal work. The past year (2023) has provided an opportunity to test the solutions scheduled for deployment. Still concerning the experts, and in the context of the goal in § 5.3 of the COP on maintaining and renewing its pool of mobilised experts, ANSES will follow up on the results from the seminar it organised in November 2023 with its experts..

More specifically, in response to a milestone of the goal in § 1.3, the Agency will be holding discussions and drawing up proposals to improve the responsiveness and relevance of the mechanism for developing health guidance values for the management of drinking water (currently the Vmax values) (see Sheet 1.3.6). These discussions will include exchanges with other stakeholders in France (the High Council for Public Health and Regional Health Agencies), in order to clearly identify their respective expectations and contributions. ANSES will also mobilise its European partners (including EFSA) with a view to encouraging the pooling of work that can be reused for managing non-compliance situations in national contexts.

In order to increase the visibility of its management of activities, ANSES has set out in Sheet 5.6.1 of the 2024 work programme how it will implement **the new strategic orientations adopted for phytopharmacovigilance for the period 2023–2028** in its projects and activities, after discussions in the Interministerial Committee between the Agency and the ministries concerned.

Lastly, a specific goal of ANSES's COP concerns governance and a strategy for data (§ 1.4). The division will help define an integrated strategy that addresses 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, or data mining for its vigilance work. Particular mention should be made of the work carried out for the "Green Data for Health/GD4H" group of the Fourth National Environmental Health Plan (PNSE4), supported by the Ministry of Ecology's General Commission for Sustainable Development (CGDD), as well as for EFSA's Advisory Group on Data (AGoD), in particular to accelerate and facilitate work to collect data for the national reporting of monitoring data in various food matrices.

2. Initiating or completing major projects

In its first theme (§ 1.2), the new COP emphasises ANSES's role in advancing the knowledge needed to assess health risks. For the division, besides the assessment methodology aspects mentioned in the previous point, this relates to the **research funding activity**. In light of the high expectations for environmental health research expressed in the PNSE4 and the goals of the COP, the Agency

presented its supervisory ministries with **a well-argued proposal to reorganise the PNR EST** and to put it forward to the Ministry of Research (see Sheet 9.3).

To demonstrate its engagement, ANSES is extending and deepening its cooperation with the ANR, by implementing the next steps of the simplification project for researchers: opening of a user space and a directory of experts (late 2023), and **development of the portal as a common platform for calls for projects** – from the submission of applications through to their assessment – which the Agency is leading jointly with the ANR. In addition, as part of the COP milestone for 2024, it **will finalise its self-assessment of the PNR EST**, which began in 2023. Along the same lines, it will also lead the drafting of the white paper for a national research strategy on occupational health. The link with expert appraisals continues to be supported, for better consideration of their recommendations in the shaping of research questions.

The Agency will work at the highest level to achieve the strategic objective of reorganising the PNR EST, taking into account the current state of discussions at the Ministry of Research which is implementing with its lead organisations the decisions taken following the Gillet mission (on organising coordination of the major research areas). In this context, a supporting mobilisation by the Agency's supervisory ministries is absolutely essential.

As part of the goals of the 2023–2027 COP (Themes 1.2 and 1.3), the division is involved in **taking on new missions entrusted to ANSES**. Preliminary work was carried out in 2023, including a proposed preparatory model for an **Indoor Environment Quality Observatory** (OQEI) and a multi-year programme drawn up jointly with the French Scientific and Technical Centre for Building (CSTB). Preliminary discussions have also taken place with the ministries – in particular the Directorate General for Health (DGS) and Directorate General for Competition, Consumer Affairs and Fraud Control (DGCCRF) – to prepare support for drafting texts and organising the transfer of **vigilance and assessment missions for cosmetics and tattoo products**. The work sheets for both the DER and the Health Alerts & Vigilance Department (DAVS) (Sheets 3.2.9, 3.5.1, 5.2.11 and 8.2.10) give an account of the work planned. However, some of this work is subject to uncertainty, as it is conditional on the granting of new resources, defined in conjunction with the supervisory ministries when the decisions were made to transfer the missions.

In 2024, there will be **three milestones for three major studies conducted by ANSES**, alone or jointly with other partners. The ChlorExpo study will be mentioned in the next part of the summary (§ 3).

For **the Albane survey** (Sheet 1.7.3), which results from combining the INCA3 and ESTEBAN studies, previously conducted separately by ANSES and *Santé publique France* respectively, 2024 will see the launch of a pilot study to **test the feasibility of the "continuous" study concept** developed jointly by the teams. This step will be carefully analysed, particularly in light of the COP goal (Theme 1.2) for ANSES to conduct a debate similar to that which led to Albane, on other studies it is leading.

For the **third Total Diet Survey (TDS3)**, 2024 will see the **roll-out of the analyses of the matrices** already sampled (Sheet 1.7.1) under the supervision of the DER's Methods and Observatories team. At the same time, the risk assessment teams are **getting ready to collect updated toxicology data** with which to prepare the risk assessments (DATA-TOX Sheet 1.3.7), which requires significant and unavoidable investment.

For the **Pesti'Riv** study (Sheet 5.7.1), also conducted jointly with *Santé publique France*, **the various components of the study should be finalised** in 2024. With regard to drawing up recommendations based on the study's conclusions, this will provide an opportunity to test a method for developing shared conclusions and recommendations (in line with the goal on the inter-agency cooperation protocol).

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); the next step in the Second National Endocrine Disruptor Strategy; 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. For the third year in a row, an annex to the 2024 work programme will focus on identifying contributing activities.

Furthermore, the following major projects should be started or completed, depending on the case, when implementing the 2024 work programme:

- Continuation of the expert appraisal responding to the formal request from all the supervisory ministries, on the risks associated with **exposure to substances in the PFAS class** (Sheet 1.3.9). After supporting the restriction project seeking to limit non-essential uses, as part of a European process led by ECHA, the DER is continuing work to identify and provide information enabling the public authorities to undertake measurements in the various environmental compartments and food matrices (water, food). Together with EFSA, ANSES has pushed for the establishment of a multi-agency group to speed up sharing of the available scientific data;
- 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 now expected to be completed in the second quarter of 2024 (Sheet 7.1). This action is being carried out with the Regulated Products Division;
- Various PNSE4 deliverables under ANSES's responsibility are scheduled for completion in 2024, including **the opinion and report on a calculation method for assessing the health and environmental hazards of household products** (Sheet 3.2.5), and vigilance with regard to plant and animal species whose proliferation may be harmful to public health (Sheet 8.2.6), with the opinion and report on processionary caterpillars;

- In nutrition, work on ultra-processed foods (Sheet 1.5.5) and the risks associated with dietary exposure to isoflavones (1.5.6) are mentioned. However, there are uncertainties around the time scales, depending on the data actually available for completing the work by the expected deadlines. In the event of any difficulties, and in line with what was mentioned above, discussions will be planned with the sponsors;
- In the area of risks associated with vectors, two major opinions are expected for 2024 (Sheet 3.3.1): the expert appraisal report and opinion on the "probability of an arbovirus outbreak in metropolitan France", and the expert appraisal report and opinion on TBE for late 2024;
- Lastly, 2024 should see the completion of several expert appraisals in occupational health exploring the risks associated with different forms of multiple exposure, particularly in the cleaning and sanitation sector (Sheet 4.4.3) and in waste recycling activities (Sheet 4.4.4).

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

The division is firmly involved in reviewing and scaling up ANSES's actions with stakeholders thanks to **the new Social Sciences, Economics & Society Department (DiSSES)** (Sheet 7.2). ANSES's work regarding openness to society will continue in 2024, under the leadership of the DiSSES, for coordination and development of the dialogue bodies, as well as the expansion of participatory research. This work falls within the scope of Theme 5 of the 2023–2027 COP "Transparent, efficiency-oriented action" and concerns in particular the milestones relating to high-quality dialogue with stakeholders (milestones: "Review of participation in dialogue bodies, 2023", "Review of citizen science initiatives, 2025 and 2027"). The recommendations of the review that will be carried out in late 2023, to be discussed by ANSES's various governance bodies (thematic steering committees, dialogue committees, Board of Administrators), will provide additional courses of action for 2024. Without waiting for this, and as part of its strategy to roll out participatory research initiatives, ANSES will experiment **by proposing meetings with research teams and members of its dialogue bodies with a view to developing innovative research projects in areas where health issues and society's expectations overlap**. Based on the experience it gained in 2023 on new genomic techniques (NGTs) and on climate change, the Agency will continue its interactions with the French Economic, Social & Environmental Council (CESE) and the National Consultative Ethics Committee (CCNE), to 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.

For the Agency, assisting with change also means **providing support for changes in the organisation of government action**. In particular, 2023 saw the **introduction of a single body to enforce health policy for food**. As a consequence, the division is currently deploying a number of different support measures: responding to a formal request on the optimisation of official controls (monitoring and control plans) in the plant sector, which were previously under the aegis of the DGCCRF (Sheet

1.3.11); preparing a framework opinion to enable the DGAL to manage most cases of marketing authorisation applications for food supplements (Sheet 1.5.8, known as "Article 18"); working on developing a generic framework for guides to good hygiene practices (GGHP) to assist authors of new guides, based on a more robust framework: this expert appraisal should also be an opportunity to redefine with the Ministry a smoother system between submission, examination by the Agency and final implementation. Lastly, in connection with the issue of data strategy and the overhaul of the corresponding information systems, the introduction of the single body to enforce health policy should also lead to a **review of the scope of ANSES's reporting of monitoring data** (see Sheet 1.8.3) to EFSA on France's behalf.

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 loss, consideration through the exposome of multiple exposure sources and substances, and changes in society's attitudes to animal welfare. The severe pressure on water resources in 2022 and again in 2023, for example, has led to three unscheduled expert appraisals to underpin changes to the regulatory framework associated with three "non-conventional" water use contexts: crops and green spaces, the agri-food industry and buildings. The challenges of conducting emergency expert appraisals on such fundamental topics illustrate the importance of anticipation in their scheduling.

With regard to *climate change*, the Agency received a number of new formal requests relating to "observable signs" of climate change with a view to preparing for adaptation to this change. These include updating the Agency's previous work on **the risks associated with the particles deposited by vegetation fires**, which can persist over very long periods, as shown by experience in other parts of the world (Sheet 5.1.2); work on the **categorisation – in terms of plant health – of eight species of exotic insects following their discovery in France** (Sheet 6.1.4); and, with a view to the forthcoming milestones for the regulation on energy consumption in new buildings (RE2020), an analysis of the **thresholds established under the RE2020 in order to determine their health consequences in terms of summer comfort** (Sheet 4.2.5).

These new formal requests have been added to a portfolio that is already well-established in other areas: **vector control** (Sheets 3.3.1 to 3.3.3), including work on adapting the monitoring and control strategy to changes in the areas where vectors are established; and the impact of wood combustion on air quality (Sheet 3.1.1). In this same context, the Agency still 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 3.4.5 for an internal request featured in its work programme since 2020).

In terms of *responding to changes in consumer expectations and behaviour*, and with regard to consumer goods, the expert appraisal of the calculation method for assessing the health and

environmental hazards of household products (Sheet 3.2.5) will be completed in 2024, as will **an assessment of the risks associated with vaping products** (Sheet 3.2.2) and a classification proposal for cannabidiol (CBD) under the CLP Regulation. In the area of food and nutrition, 2024 should see the drafting of an initial opinion on nutritional guidelines for vegetarian diets (Sheet 1.5.2) and another on **characterising and assessing the health impacts of consumption of ultra-processed foods** (Sheet 1.5.5). In animal nutrition, **changes in practices have been observed, with a tendency to give mainly carnivorous pets new foods** (vegetarian foods, BARF, etc.), whose risks to animal health should be assessed (Sheet 2.3.3).

Lastly, in terms of support for societal challenges, the work programme includes a series of actions that reflect **ANSES's efforts to support the French Caribbean population**, who are faced with long-term persistent chlordecone contamination. As was noted at the symposium in late 2022, the opportunities for acting on knowledge of exposure and its reduction are key tools for improving the situation: individual chlordecone blood levels, soil measurements, etc. The **ChlorExpo study is due to be completed in 2024** (Sheet 1.7.2) and will provide useful information on how to further reduce chlordecone levels in food through preparation and cooking methods. In addition, the Agency will be respectively initiating or continuing work on two formal requests (Sheet 1.3.8): the first will seek to introduce a food control policy to monitor reductions in levels following actions undertaken to this end; the second involves cooperation between the DER and the DiSSES to propose a tool for optimising the use of soil according to its level of contamination.

Anticipating emerging threats and risks is a major theme of the new 2023–2027 COP (Theme 2), which is being supplemented by a section on preparedness for emergency or crisis situations. A practical illustration of this strengthening of preparedness is provided by **the specific sheet on preparations for the 2024 Olympic and Paralympic Games** (Sheet 8.2.11), which includes risk mapping, drafting of risk sheets and action plans in conjunction with the DGS's working group, and organisational measures such as a review of ANSES's on-call arrangements and other practical aspects of internal organisation (teleworking or transport to the site for the laboratory staff concerned, etc.).

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, are already an important resource for identifying emerging threats. Indeed, these platforms identified the recent emergence of epizootic haemorrhagic disease in south-west France in autumn 2023, whose progress will be closely monitored.

In terms of avian influenza, the epizootic management landscape is set to change significantly with the implementation of a proactive vaccination policy from autumn 2023. Working with *Santé publique France*, the ANSES teams will nevertheless remain vigilant to any changes and mutations that the virus is likely to undergo as it jumps between different animal species, in both wildlife and domestic livestock. Maximum attention must be paid to identifying any mutation that could transform this epizootic virus into a zoonotic virus, transmissible to humans and capable of human-to-human transmission.

Regarding vigilance in plant health, mention should be made of continuation of a project under an agreement with EFSA (Sheet 6.2.1) in which ANSES is helping to set the parameters for the MediSys information search platform, in order to ensure **automated monitoring of the media and scientific literature for identified quarantine pests** and new plant pests.

Lastly, as part of its work coordinating the vigilance schemes, which will be expanded in early 2024 to include cosmetovigilance as part of the new missions assigned under the 2023–2027 COP, the DAVS will launch a debate into measuring the satisfaction of the "customers" of the various vigilance schemes, with a view to improving the service provided.

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 2024, 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 early 2024, 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: the first day of scientific conferences for 2024 will be devoted to research funded by the programme, focusing on endocrine disruptors and their effects on health and the environment;
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.

In terms of institutional relations, a major point for 2024 in terms of **renewing partnership agreements is the one between *Santé publique France* and ANSES**. This covers a broad range of

projects and areas of cooperation, and will aim to highlight how this cooperation constitutes **a hub for designing and deploying actions as part of a "One Health" approach**.

5. Europe and international

These actions are generally coordinated within ANSES by the European & International Affairs Department (DAEI) and are in line with Theme 4 of the 2023–2027 COP goals. Some of them are managed by the division's entities or call heavily on their resources, in accordance with the general strategic orientations. The specific features of European action in 2024 are set out below.

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.

With a change of mandate at the European Parliament due in the first half of 2024, uncertainties remain about the changes to the regulations/directives in preparation that will take place before the new mandate. These concern the CLP Regulation (on classification, labelling, packaging) with its new hazard classes having now been adopted, the text on NGTs, and the plan to develop the REACH Regulation. Of course, each time a draft text falling within the Agency's remit is prepared, ANSES's scientific teams are called on – together with the French authorities – to analyse the relevance of the proposed provisions with regard to health issues. One of the key points requiring attention, in relation to the **development of the REACH Regulation**, concerns the **conditions under which *in vivo* tests can be replaced by *in vitro* tests, in line with the 3R approach** (replace, reduce, refine) seeking to reduce the use of tests on laboratory animals. While it is entirely legitimate to optimise the use of animal testing, increased expectations for **reliable characterisation of substance hazards** and the complexity of new hazard classes (such as endocrine-disrupting substances) mean that substitution is not possible without verification. The division will work in a cross-functional way within the Agency, but also by seeking links with the other agencies/institutes concerned, to distinguish relevant changes from those needing further validation.

The entry into force of these new regulations will 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 5.2.2 to 5.2.10).

Late 2023 and early 2024 will see the **start of the assessment partnership project under the aegis of EFSA, relating to the risk assessment of food enzymes, food flavourings, and food and feed additives** (Sheet 1.3.10). The aim is to establish long-term cooperation (4 years) with one or more selected recognised organisations. It involves supporting EFSA in the preparation of its scientific opinions on certain chemicals regulated at European level. The project has been organised by EFSA in the form of a Framework Partnership Agreement (FPA). The **consortium includes numerous European partners**: Austrian Agency for Health and Food Safety (AGES, Austria), National Food Institute, Technical University of Denmark (DTU, Denmark), German Federal Institute for Risk Assessment (BfR, Germany), University of Thessaly (Uth, Greece), National Institute for Public Health and the Environment (RIVM, Netherlands), Norwegian Institute of Public Health/Norwegian Scientific Committee for Food and Environment (FHI/VKM, Norway), Norwegian Institute for Marine Research (IMR, Norway) Swedish National Food Agency (Livsmedelsverket) (SFA, Sweden). **The**

success of this project is strategic in two ways: practical application of the partnership concept over the long term to optimise scarce risk assessment resources at European level; viability of the partnership model designed by EFSA in scientific terms and with regard to model sustainability.

The other component is the fully operational implementation of 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, new and emerging 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 (Sheet 5.7.2).

In addition to the PARC partnership, the division is also likely to be involved, albeit to a lesser extent, in other projects and partnerships being set up in ANSES's field, whether in sustainable food or animal health and welfare, in line with the strategic orientations for research on risk assessment (see § 1).

Regarding work in partnership with our European counterparts, ANSES is the lead French entity (with other partners such as *Santé Publique France*, French National Cancer Institute and the DGS) of two European Joint Actions, co-funded by the European Union's 4th Health Programme “EU4Health”:

- Following on from the Best-ReMaP Joint Action on implementation of validated best practices in nutrition, which ended in 2023, ANSES will coordinate the "Support public policies to promote food reformulation" sub-task in Work Package 5 (Regulation and taxation) of the European joint action on prevention of non-communicable diseases (JA-PreventNCD project);
- 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.

Regulated Products Division

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

- **Plant protection products** (PPPs);
- **Biocides**[56];
- **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[57] and CLP[58] 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 2024 work programme of the Regulated Products Division will be structured around the following framework elements:

- **Continue improving the efficiency observed in 2022–2023**, by looking for ways to optimise assessment and decision-making processes to help achieve appropriate examination times for applicant dossiers, particularly regarding plant protection products; this goes hand in hand with maintaining efficiency when the indicators are already highly satisfactory (as is the case with veterinary medicines);
- **Maintain responsiveness for work on formal requests**, particularly in the event of alerts or emergency situations reported by the bodies issuing the requests, while striking a balance with work on application dossiers, the division's core activity;

[56] 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.
[57] 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.
[58] Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures (known as the CLP Regulation).

- **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 the European Chemicals Agency (ECHA), European Medicines Agency (EMA) and European Food Safety Authority (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**;

    - Contribute to the implementation of measures taken in the framework of the National Sovereignty Plan for the fruits and vegetables sector;

    - Provide input for the debate on the **Ecophyto 2030 plan by contributing to this plan's Scientific and Technical Committee** (Science for Expertise Division) and to questions on the determinants of this plan's indicators; in this regard, an ANSES commitment note was produced in 2023, setting out certain levers for reducing PPP use;

    - Be a stakeholder in **EcoAntibio** through the contribution of the ANMV[59] to 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;**

    - 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 European Commission's Chemicals Strategy for Sustainability, which is the European deliberation on "One substance, one assessment" issues.

    - Contribute to the Fourth National Environmental Health Action Plan (PNSE4) on issues relating to the proper use of biocidal products.

- **Strengthen information sharing and maintain listening and dialogue**, in particular by perpetuating the **platform for dialogue** on marketing authorisations (MAs) for PPPs (the chair of this body is expected to be renewed) and by coordinating the day of meetings with veterinary medicine stakeholders;

[59] French Agency for Veterinary Medicinal Products, within the Regulated Products Division.

- Maintain an **activity and presence at 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 FAO/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 main 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[60].

This activity is mainly financed by tax revenues or fees, which depend on the volume and type of applications submitted. A major issue is therefore ensuring an appropriate level of taxes and tax rates, in view of the costs borne by the Agency. After revising the tax rates for VMPs, the division will continue to work with the Legal Affairs Department on the tax rates for PPPs and to examine its business model with a view to stabilising the rates over several years and adjusting them to the workload and inflation, while ensuring that the biocontrol strategy is not held back.

Adjustments to the information systems

Modernisation and digitisation through information systems (ISs) are contributing to overall efficiency. To this end, in the area of biocides, the SIMMBAD platform was replaced in early 2023. A specific IS for managing the examination of biocide applications, 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[61]) and the IS department of the

[60] Parallel trade permits; authorisations by mutual recognition, etc.
[61] Regulated Products Assessment Department and Market Authorisations Department within the Regulated Products Division.

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 for plant protection products, and will be further developed to eventually include a tool for managing the submission of application dossiers. The European PPPAMS[62] 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 redundancy of tasks and tools. Lastly, software applications relating to veterinary medicinal products now exchange data with the European databases developed by EMA under the new Regulation (EU) No 2019/6, since its entry into force on 28 January 2022, with the creation of the Union Product Database (UPD). 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.).

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-assessments of ASs or assessments of new ASs) and MA renewals, as well as the submission of other applications including new MAs, parallel trade permits (PTPs), etc. For 2024, 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 a hundred applications processed per year since 2017;
- Optimize the schedules for granting authorisations to market products by taking into account the constraints linked to the crops calendar and to the essential uses in compliance with the zonal evaluation procedure.
- Backlog reduction trajectories maintained for PPP dossiers, and processing times maintained or improved for all regulated products.
- Prioritisation of dossiers for biocidal active substances that have not yet been approved, to help speed up the procedure for examining existing substances and with a view to meeting the new deadlines set by the European Commission. To this end, the teams are expected to be strengthened under an agreement on funding until 2028 that has been signed between ANSES and the European Commission.

[62] Plant Protection Products Application Management System https://food.ec.europa.eu/plants/pesticides/authorisation-plant-protection-products/pppams_en

Milestones in the 2024 expert appraisal trajectory

This section focuses on the methodological aspects related to changes in the assessment framework, which are particularly important for tailored assessments.

- **Methodological developments and scientific cooperation**: **here 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 Section 5 of this summary.**

  Another key point is cooperation with EFSA in 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 will require a CRA, as well as in methodologies for assessing non-dietary exposure to PPPs, and lastly, 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, the priorities identified for 2024 are as follows:

  Regarding innovative therapies:

  - finalise the assessment requirements drawn up by the ANMV for establishments offering veterinary phage therapy, and implement them in France;
  - draft guidelines for assessing applications for monoclonal antibodies (focusing on pharmaceutical quality and pharmacokinetics), in order to be ready in 2024 to assess applications through the centralised procedure for EMA;

  Regarding phytotherapy:

  - apply the methodology for setting maximum residue limits (MRLs) for plant-derived products, based on the examples of tea tree and Mexican tea essential oils, and lead the regulatory and scientific work packages of the European COST project MEDPLANT4VET, in order to extend the scope of the work carried out;

  Regarding antiparasitics:

  - monitor the results of the Fipronil study and ensure they are addressed at European level;
  - take part in the launch of the AMPARA project and act on the recommendations of the formal request on antiparasitics applied in dips, showers and sprays that relate directly to the ANMV's work;

Regarding alternatives to clinical trials:

- using the literature and a survey of professionals, draw up an inventory of alternative methods to clinical trials – new approach methodologies (NAMs) – for assessing the toxicological component of veterinary medicinal product dossiers, which will include an inventory of regulatory tools for taking better account of NAMs in assessments.

Milestones in the decision-making process

It should also be noted that, as a decision maker, ANSES has to perform essential tasks that are unrelated to expert appraisal, such as 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;** buffer zones to protect local residents from CMR2 products, on dossiers submitted;
- Decisions made available 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;
- The coming year will also see the DAMM's analysis of the conclusions of the expert appraisal on **plant protection products containing the active substance copper,** and 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). In 2023, the mandatory comparative assessment for this AS approved as a candidate for substitution was carried out under Article 50.1 of Regulation (EC) No 1107/2009;
- 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), or signals collected from other vigilance schemes, as well as its interactions with *Santé Publique France*, 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 (biomarkers) or environmental monitoring studies.

The PestiRiv study is continuing, with sampling having been carried out correctly in 2023.

Following on from the GEOCAP-AGRI project, ANSES was keen to extend knowledge of the links between occurrence of paediatric cancers and pesticide exposure in agricultural areas. The Agency will therefore fund a team from Inserm to carry out **the GEOCAP-PEST study**, which will seek to **characterise exposure** to pesticides from the use of plant protection products in crop-growing areas.

ANSES's work will also focus on improving knowledge 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 may be taken on MAs if warranted by the risk, like the amendments made on S-metolachlor in 2022, for example.

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.

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 PPP, the MA monitoring committee has already been asked to address issues such as S-metolachlor and prosulfocarb. For VMPs, the mandate of the members of the corresponding monitoring committee (CSMV) was 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 PPP expertise to State control bodies.

It will also carry out inspections of product formulation facilities in line with its resources (two FTEs) 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 facilities or activities now subject to the obligations of Regulation (EU) No 2019/6 or the French Public Health Code, through a 2024 inspection programme based on risk analysis; continuation of the Europe-wide review of good manufacturing practices for veterinary medicinal products and autogenous vaccines; adoption of new guidelines for good laboratory practices or good clinical 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 PPP 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 of the presence of certain metabolites in water analysed by the PPV scheme, such as 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 made to 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 consumer products**, in order to clarify their labelling (planned for late 2023);
- Management measures in the event of **botulism** in wildlife (biocidal issues);
- **Stinging caterpillars**: health risk analysis/management recommendations;
- Support for the **Vectors Mission with regard to vector control methods**.

The main expert appraisals to be led by the division in 2024 are as follows:

- **Exposure to succinate dehydrogenase inhibitors (SDHIs): the opinions issued on 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 will be communicated at European level.**
- Request for scientific and technical support to the inspection authorities for determining a limit value for *Legionella longbeachae* in fertilisers and growing media.
- 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 MRLs in interaction with ANSES's working group on "Plants" (internal requests on tea tree and Mexican tea essential oils used as antiparasitics).**

In 2024, the Regulated Products Division will contribute to expert appraisals led by the Science for Expertise Division, such as the internal request concerning the characterisation of chemical dangers and the selection of their most relevant toxicological reference values for assessing risks linked to food.

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 twice a year with a new Chair. This body 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[63] are published on the ANSES website. 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 be organising its 30th anniversary, combined with a day of meetings for the Agency's stakeholders, representing the entire veterinary medicinal products chain from veterinary pharmaceutical manufacturers and wholesalers through to veterinarians and breeders, in the second quarter of 2024.

[63] Reports and decisions regarding MAs for biocidal products are also published, but on the ECHA website.

5. Maintain and develop the Regulated Products 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 on active substances in 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[64]) and international (CCPR[65]) levels for plant protection products; in the BPC[66], CG[67] and in meetings of the competent authorities and the SCBP[68] for biocidal products; through participation in EPPO's[69] herbicide panel; and in the EMA's standing committee on veterinary medicinal products (CVMP[70]) and expert group on veterinary medicinal products (CMDv[71]) for veterinary medicines. It also provides support to the competent authorities in setting standards for fertilisers.

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

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[64] SCoPAFF: Standing Committee on Plants, Animals, Food and Feed. A regulatory committee chaired by the European Commission.
[65] CCPR: Codex Committee on Pesticide Residues.
[66] BPC: Biocidal Products Committee, under the European Chemicals Agency (ECHA).
[67] CG: Coordination Group for Biocidal Products, for which ECHA provides the secretariat.
[68] SC: Standing Committee on Biocidal Products.
[69] EPPO: European and Mediterranean Plant Protection Organisation.
[70] CVMP: Committee for Veterinary Medicinal Products.
[71] CMDv: Coordination Group for Mutual Recognition and Decentralised Procedures – Veterinary.

Cooperation, 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);
- Updating of EFSA's methodology for assessing non-dietary exposure to plant protection products (management of a consortium of institutes and universities);
- 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 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;
- Participation in the development of environmental assessment methods for disinfection by-products (biocides).

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 third mandate in 2023) and by continuing its commitment to the network of **European Heads of Medicines Agencies** (HMA).

Through its mandate as a WOAH Collaborating Centre in 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 European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) scheme led by the EMA and to actions on **resistance to antiparasitics**. It will also be leading the VETFRAM project, funded by the European Commission over six years. This intends to use the Calypso application to organise declarations of antimicrobial use reported by the various animal production sectors at European level, in order to provide input for the new Antimicrobial Sales and Use (ASU) database.

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

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