ANSES 2022 work programme

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I. General orientations

ANSES's work programme for 2022 is in line with the strategic orientations drawn up in late 2018 and since updated for each of the Agency's fields of activity, and is consistent with its 2018-2022 goals and performance contract ("COP" in French) and with the Agency's ambitions set out in the ANSES 2025 document:

- food safety and nutrition;
- animal health and welfare;
- environmental health;
- plant health and protection;
- occupational health.

The deployment of these orientations contributes to a vast array of national or sectoral plans in which ANSES is involved at different stages: formulation of proposals before they are adopted or developed, coordination of certain initiatives or mobilisation for others. These include the recently adopted 4th National Environment & Health Action Plan (PNSE4), the 2nd National Endocrine Disruptor Strategy (SNPE2), the 4th National Occupational Health Plan (PST4), the National Nutrition and Health Programme (PNNS) and the associated national food plan (PNA), the Chlordecone 4 plan, the roadmap to tackle antimicrobial resistance, the Ecophyto 2+ plan, the National Plan for Adaptation to Climate Change (PNACC2), etc. National strategies such as the ten-year Cancer Prevention Strategy and the National Strategy for Biodiversity are also concerned. An annex to the work programme explains these contributions.

These orientations also aim to address strategic challenges at European level: the European Green Deal and the resulting initiatives, primarily 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. In addition, ANSES's work is in line with the European One Health action plan to combat antimicrobial resistance, the Pharmaceutical Strategy for Europe, and Europe's Beating Cancer Plan, as part of the EU's health programme (EU4Health).

Active in seven fields of investigation – food, epidemiology & biomonitoring, antimicrobial resistance, exposure & toxicology, plant health, animal health & welfare, and occupational health – ANSES's cross-functional scientific departments work to reinforce the coherence of the Agency's actions by boosting cooperation between its research, reference and surveillance activities, and strengthening synergies between these activities and other Agency missions, in particular risk assessment and vigilance.

The 2022 work programme consolidates the way in which ANSES addresses several challenges, in all its missions and activities, that reinforce its role as both a reference player and a source of ideas, in support of its usefulness for the public authorities and all risk stakeholders:

- **Continue acquiring knowledge on risks to support expert appraisals.** The aim is to use the exposome to better identify the health consequences of exposure, understand changes in consumption habits and behaviour, and take better account of sensitive or vulnerable populations, with a view to improving health risk assessments for all types of agents – whether chemical, physical or biological – and the investigation of new factors (societal, organisational, etc.).
- **Contribute to the development of scientific methods and tools that improve risk detection and characterisation** (for example cumulative risks associated with combinations of chemicals), reduce uncertainties (for example on identifying and attributing pathogen sources) and integrate new approaches, especially in terms of socio-economic assessment.
- **Anticipate, identify and characterise health risks, including during crises**, by continuing to develop surveillance and vigilance systems, ensuring in particular that emerging risks are properly understood, and by developing epidemiological models that help sustain the Agency's expertise.
- **Develop an integrated approach to risk assessment**, as part of a One Health approach in the field of zoonoses for example, or One Welfare in the fields of animal welfare and occupational health, taking the complexity of situations into account, especially since they underlie subjects being debated in society. The Agency is also stepping up its commitment to risk prevention and reduction policies, and is helping to make information more widely available. It is actively contributing to research on emerging diseases by integrating this One Health dimension into the national and international programmes that emerged during the COVID-19 pandemic.
- Reinforce ANSES's commitment to improving its efficiency regarding **better management of deadlines for regulated products**.

- In early 2022, complete the transfer to ANSES of some of the assessment tasks assigned to the **High Council for Biotechnology (HCB)** as well as the consolidation of the Agency's expertise on **socio-economic analysis**.

The COVID-19 crisis has confirmed the need for a more global and effective assessment of health risks. ANSES therefore actively ensures that its work takes place in a European and international dimension. This consolidation, concerning its reference and risk assessment activities and its work on regulated products, has led it to step up its participation in major European research projects and partnerships, which have been made possible by Horizon Europe, the ninth European framework programme for research and innovation, which took over from its predecessor, Horizon 2020, on 1 January 2021.

The Agency will have three main priorities at European level in 2022:

- **Involvement in major European research partnerships under Horizon Europe.** ANSES has been lined up as coordinator of the Partnership for the **Assessment** of Risks from Chemicals (PARC), which was planned in the first wave of partnerships launched under Horizon Europe. It is intended to provide chemical risk assessors and risk managers with the data, knowledge and methods required to address current, emerging and new challenges in chemical safety. Subject to the European Commission's approval of the application submitted by a consortium of 200 partners from 28 countries and three European agencies, ANSES will coordinate the scientific, administrative and financial aspects of the project, which will receive €400 million in funding over seven years and whose ambition is to structure public scientific action on chemical risks on a European scale.

  Several other Horizon Europe projects, following on from the work of the One Health European Joint Programme (EJP) coordinated by ANSES, are also of major strategic interest. These include the partnership on animal health and welfare, in which ANSES has a leading role within the European working group tasked with preparing it; the partnership on antimicrobial resistance, in line with the One Health approach; and lastly the partnership on safe and sustainable food systems. As these three partnerships are on the European calendar for 2023/2024, ANSES's involvement will go ahead according to the opportunities it can arrange and the resources it is able to mobilise.

- **Involvement in activities for the French Presidency of the Council of the EU ("PFUE 2022") in the first semester of 2022**: ANSES will be leading various actions and initiatives of its own during this period (such as hosting meetings or organising events), and will be contributing to those of its partners and the French authorities.

- **Strengthened ties with the various EU agencies, as well as greater visibility and communication on ANSES's work and relations with these agencies**: numerous ANSES entities work closely with the competent EU agencies in our areas of activity. These activities have been ramped up, particularly with regard to the European Food Safety Authority (EFSA) and the new Regulation (EU) 2019/1381 on the transparency and sustainability of the EU risk assessment in the food chain. Within the framework of working groups or consultations on European regulations, in 2022 ANSES will also be attentive to and active in implementing certain strategic priorities of the Green Deal that are of particular importance to ANSES, such as the "one substance, one assessment" approach, the inclusion of hazard classes for endocrine disruption in the CLP Regulation, and the requirements on data for risk assessment.

Against a backdrop of growing interest and concern about health issues, in 2022 ANSES will also continue its efforts to make its scientific conclusions and recommendations accessible and to 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, with specific attention paid in 2022 to fostering a good understanding and dialogue on its forthcoming new missions in the field of biotechnologies.

II. Strategic orientations

Food safety and nutrition

Animal health and welfare – Animal nutrition

Environmental health

Plant health and protection

Occupational health

Food safety and nutrition

Preamble

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

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

Food must now be **"healthy, safe and sustainable"**; it must cover all these dimensions along the farm to fork supply chain, including environmental aspects. In addition, new topics are being considered, such as **food waste** or the issue of **food contact materials**, especially plastic packaging. These topics have taken on added significance recently with the health crisis, where it has been necessary to review and adapt methods of food production and, in particular, food distribution to consumers.

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

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

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

THEME 1 – Strengthen control of health risks to ensure safe food

The recent health crises due to chemical or biological contaminants, on which ANSES continues to deploy considerable efforts, are a sign that **controlling food-related health risks**, even those that are well-known, remains a fundamental challenge for public authorities and consumers. This control of health threats necessarily involves a risk assessment process serving several objectives.

- **Identify and characterise hazards using innovative approaches**

Within the Agency, documenting hazards relies on both the actions of ANSES laboratories, as part of their reference and surveillance activities or specific research work, and the activities of the Risk Assessment Department. The actions of ANSES's laboratories are detailed in the laboratory work programme and will soon be assessed as part of the collective audit scheduled for January 2022.

In 2022, ANSES will actively pursue its **analytical reference** missions, with 17 national and three European reference mandates in food safety, including drinking water, to which a new mandate for SARS-CoV-2 in wastewater and sewage sludge has now been added.

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

The **deployment of new analytical techniques**, which is a priority, will be continued and expanded. For biological hazards, this reinforces genomics and metagenomics techniques and also considers more broadly all "omics" type technologies, as well as the associated development of tools for detecting and identifying markers of interest for public health using high-throughput qPCR.

High-resolution, multi-residue, non-targeted mass spectrometry techniques for chemical contaminants from natural, anthropogenic or multiple sources will be used to extend knowledge of the exposome. This will enable ANSES to actively contribute to identifying and characterising hazards through the **constant improvement of analytical methods,** in terms of performance (specificity, reducing limits of detection and quantification, chemical speciation, etc.) and innovation (non-targeted approaches) for the identification of **new or emerging** contaminants (foodborne viruses, non-regulated substances in water such as metabolites of pesticides or plant protection products, etc.), while broadening its scope to all food matrices.

ANSES will also be documenting the **characterisation of hazards** through the detection of **virulence markers** or pathogenicity elements (characterisation of bacterial toxins, marine biotoxins, infectivity in virology, adhesion or biofilm formation ability, virulence factors of enterohaemorrhagic *E. coli, Listeria monocytogenes*, etc.) or by producing data on **host-pathogen relationships** thanks to the laboratories' research activities and the risk assessment work of the expert groups.

Work on molecular characterisation of the resistome and of genetic carriers of **antimicrobial resistance** determinants in different environments will be pursued as part of national and European projects.

The Agency's work on *in vivo*, *in vitro* and *in silico* toxicology will help produce new knowledge for the characterisation of chemical hazards. Extensive work will be carried out by the Risk Assessment Department to update the methodology for developing **health reference values**. ANSES will also continue developing analytical methods to characterise new hazards (quaternary ammoniums and triamine, biogenic amines, microplastics, plastic additives) in food products and water (explosives residues, 1,4-dioxane, plant protection products and metabolites). Exploratory measurement campaigns will produce data on contamination levels that will be used for ongoing or future risk assessment processes at the national and European level.

The issue of analytical data storage, accessibility and reprocessing will be addressed in the framework of the ANSES for Open Science strategy. Lastly, the Agency will pursue its integrative approach to chemical risk assessment by strengthening its ability to detect and characterise hazards, assess exposure, and monitor and control these threats.

- **Structure surveillance and data collection**

The structuring of epidemiological surveillance relies heavily on deployment of the surveillance platform for the food chain (**SCA Platform**) and the associated epidemiological methodologies (source attribution of infectious foodborne diseases, comparison of strains, phylogeny, trend analysis, etc.) and exposure science methodologies (ranking of chemical hazards). In 2022, these approaches will provide information on the prevalence and development of various known, emerging or re-emerging contaminants within the various food production, processing and distribution sectors, the ultimate goal being to anticipate and control risks.

With the help of all its partners, the SCA Platform will contribute to data analysis through descriptive epidemiology work mainly using prevalence data, or analytical epidemiology in order to identify circulating virulence clusters or clones, reservoirs and food vectors of disease. Structuring surveillance also requires the quality of the stored data to be improved (format, validation) so that they can be made available for risk assessments.

The consolidation of ANSES's role as the **interface with EFSA** and the data quality missions will remain essential actions (maintaining and improving the flow of data from the CONTAMINE database; extending the QUALIPLAN project to a greater range of data in order to improve their exploitation; participating in EFSA's ad hoc scientific networks). In this context, ANSES will be involved in work arising from application of the Report of the Advisory Forum Task Force on Data Collection and Data Modelling[2] coordinated by EFSA's Advisory Forum Task Force, mainly to implement certain recommendations in conjunction with the national players concerned.

[2] EFSA (European Food Safety Authority), Alvarez-Pinera J, Bager F, Bystrický M, Ditmann Rasmussen S, Foster D, Fuchs K, Gilsenan M, Grahek-Ogden D, Jozwiak A, Sanaa M, Neagu M, O'Dea E, Perrella A, Richardson J, Scharfenberg E, Sokolic D, Stack M, Vermeersch K, Wienk

- **Document overall exposure and assess health risks**

Total Diet Studies (TDS), conducted at regular intervals (approximately every six to 10 years) with a specific approach each time that focuses on new hazards or particular populations, are designed to estimate dietary exposure to numerous chemicals found in foods (numerous PPP[3] residues, FCM[4] migration products, etc.). These studies are essential for providing information on exposure, associated risk levels and trends.

ANSES will help consolidate achievements here by carrying out **a third TDS**, which will examine a defined number of substances, with a specific focus on organically-grown food. The coming year will be devoted to completing the field phase of food sampling, selecting laboratories capable of analysing the targeted matrices while complying with the analytical limits necessary for health risk assessments, and initiating these analyses. At the same time, work will be undertaken to investigate and select the health-based guidance values to be used for the substances included in the TDS3.

ANSES is also carrying out a specific study in the French Caribbean (ChlorExpo), with a methodology similar to that of the TDS, to acquire data on contamination and conduct exposure calculations with a view to assessing the dietary health risks of chlordecone and its main metabolites.

- **Continue ranking hazards and foods posing a risk**

The recommendations of the Interministerial Committee for the modernisation of public administration (CIMAP) highlighted the need to better inform public decision-makers by proposing a **ranking of biological and chemical hazards, in order to rationalise control and surveillance priorities**. To this end, ANSES has undertaken extensive work **for the third component of CIMAP**. Encompassing all food hazards, the purpose of this work is to create a system for ranking hazards and their food vectors, taking very different hazards into account in an integrated way.

As a follow-up to this work, ANSES plans to establish the criteria defined to rank one or more food categories and draw up a list of hazards for each production sector based on these criteria. This methodology will also be applied in expert appraisal work on controlling risks associated with the presence of Enterobacteriaceae in raw milk cheeses.

THEME 2 – 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 obesity epidemic remains a particularly worrying warning sign, and situations of sedentary behaviour increased during the lockdown due to the health crisis. In this area, ANSES offered a variety of measures and proposals.

- **Identify food composition and the food supply: OQALI and Ciqual**

A balanced diet requires the right individual habits but also that the foods offered to consumers have an adequate nutritional composition. Improving the quality of the food supply is therefore an essential part of nutrition policy. **The French Food Observatory (OQALI)**, run jointly with INRAE, contributes to this goal by providing a unique source of data on food quality, including monitoring of the Nutri-score nutritional labelling system. Future plans include improving visibility of the OQALI database, conducting initial monitoring in 2022 of the possible impacts of Nutri-score deployment on ready-meal reformulation, and rolling out the OQALI model at European level as part of the European Best-ReMaP Joint Action on implementation of validated best practices in nutrition.

ANSES manages a public database detailing the average nutritional composition of foods consumed in France; this **Ciqual** table is one of the most comprehensive in Europe. It will be updated in 2022 to include more recent composition data for processed products (from OQALI), levels of added/free sugar, as well as isoflavone levels in foods consumed in particular in vegetarian diets. Analysis campaigns will continue in order to keep up the input of new high-quality data.

K, 2020. Report of the Advisory Forum Task Force on Data Collection and Data Modelling. EFSA supporting publication 2020:EN-1901. 63 pp. doi:10.2903/sp.efsa.2020.EN-1901. https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/sp.efsa.2020.EN-1901

[3] Plant protection products

[4] Food contact materials (packaging, etc.)

- **Document the influence of cultural behaviours and determinants**

The quality of the food supply is a determinant of nutritional quality, but other factors are equally essential. ANSES will help document the extent to which physical activity or the level of sedentary behaviour are in line with the health guidelines in this area. This topic has become more important since management of the health crisis has led to new working habits that are expected to endure. ANSES will pay particular attention to the consequences in terms of physical activity and sedentary behaviour. It will also work on burning issues concerning the rate and quantity of food intake and their influence on health parameters. Contributions from the human and social sciences are often essential here; expertise in social and economic sciences is expected to become increasingly important in ANSES's work.

- **Inadequate nutritional intakes: assess risks and contribute to the PNNS[5]**

ANSES will draw on data collected in the Third Individual and National Study on Food Consumption (**INCA3**), a recurring survey, to estimate food consumption, nutritional intakes and dietary exposure to chemical contaminants. The Agency will develop harmonised statistical and IT tools and calculation practices for quantitative risk analysis. As part of the PNNS, ANSES will facilitate the exploitation of its conclusions on **consumption guidelines** for all populations and, in particular, in 2022-23, people following diets excluding some or all foods of animal origin, including vegetarians, and physically active populations (athletes, workers, etc.). This provides the public authorities with invaluable support and a scientific basis for the messages developed and then relayed by *Santé publique France*.

THEME 3 – Anticipate new risks and trends to ensure evolving and integrated assessments

- **Build the methodology for tomorrow's risk assessments**

It is important to develop knowledge on aggregate exposure (taking different routes of exposure into account) and on exposure to mixtures (cumulative exposure), including for hazards that have already been documented. Toxicological questions are increasingly being added to purely nutritional ones. New scientific questions are emerging, such as the role of the exposome in the development of chronic diseases and 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 implementation of tailored risk assessments.

This will primarily include:

- methodological work on **exposure factors**, differential identification of risks to **specific populations**, including consideration of specific sensitivities;
- development of methodologies for exploring **aggregate and combined human exposure to chemicals** with a view to assessing risks;
- identification of the major routes of exposure to cadmium, and tools for reducing population exposure through an integrated risk assessment approach;
- development and improvement of new methodological approaches (*in vitro*, *in silico*) for hazard characterisation;
- analytical methodological developments in the context of the forthcoming TDS study (speciation of trace elements, single-residue methods for pesticides);
- for biological hazards, a **"multi-hazard" approach per production sector** and source attribution of infectious foodborne diseases;
- development and improvement of **physiologically-based toxicokinetic (PBTK) models** in order to refine risk assessments;
- a more thorough investigation of **biomonitoring** issues (definition of relevant markers and setting of critical blood concentration values, etc.), with a leading role in the European human biomonitoring project, HBM4EU, due to end in 2022, and in a future partnership project co-funded under Europe's Horizon Europe Programme, the Partnership for the Assessment of Risks from Chemicals – PARC (2022-2029).

[5] PNNS: French National Health and Nutrition Programme

- continuation of assessments of **endocrine disruptors** as part of the 2nd National Endocrine Disruptor Strategy (SNPE2) and the 4th National Environment & Health Action Plan (PNSE4);
- development of **harmonised statistical and IT calculation tools** for quantitative risk analysis;
- proportionate consideration of **uncertainties and levels of evidence** in risk assessments.

- **Learn more about new risk factors and then adapt the risk assessments**

The INCA studies provide consumption data essential for the assessments mentioned previously in Themes 2 and 3. In addition, particularly since the most recently published study (INCA3, 2017), they have enabled information to be collected on **new consumption or lifestyle habits and patterns that influence diet**.

In conjunction with *Santé publique France*, ANSES has been considering the approach to be taken for jointly conducting a **new INCA4 study that responds to the recommendations** made during previous expert appraisals, particularly on the specific consumption characteristics of certain population groups. In this context, ANSES needs to identify new practices or growing trends where risk assessments need adjusting, define their possible health impacts and maintain effective vigilance mechanisms, taking the TDS3 study into account. New risk factors have thus been identified (consumption of raw animal products or foods after the recommended consumption dates), along with new products from organic farming, and specific diet types (vegetarian, vegan). ANSES will remain attentive to new products, technologies, recipes and consumption patterns. Particular attention will be paid to **novel foods** within the meaning of the legislation: foods resulting from GMOs (by developing risk assessment in addition to the examination of individual applicant dossiers), "nanos" used in foods, newly-formed substances, and herbal food supplements, whose consumption is increasing sharply.

ANSES's laboratories take a holistic approach to their work to consider changes in production, processing, distribution and consumption methods, in order to identify, quantify and characterise the impact of these changes on product safety and potentially on microbial or chemical contaminants. Studying **the influence of the microbiota** at different levels (influence on antimicrobial resistance, interaction of commensal and pathogenic bacterial communities, relationship between nutritional quality and health-promoting microbiota, etc.) and its inclusion in the Agency's work on food risks and benefits may be considered.

- **Vigilance and emerging threats**

ANSES will maintain a high level of alertness with regard to certain foods, **through its Nutrivigilance and Toxicovigilance schemes** (coordination of the CAP-TVs[6]) and the competence of its working group of experts on plants. These schemes have already identified several adverse effects associated with the consumption of certain food supplements.

The **Phytopharmacovigilance** scheme set up at the Agency is an invaluable tool for the post-MA management of **plant protection products** and the identification of their possible impacts, particularly in the food sector.

- **Coordination of health alerts**

The Agency **coordinates the collection of health signals and alerts** in its fields of competence in conjunction with the players involved and external partners (DGS, DGAL, DGCCRF, etc.). A weekly internal alert report is prepared for the Agency from the **SALSA register**. ANSES's alerts on human health are forwarded to the Directorate General for Health and discussed at the Ministry of Health's weekly meeting on this topic.

- **Move towards more integrative assessments to achieve "healthy, safe and sustainable" food**

A forward-looking debate (feasibility, priority topics) on taking the **overall impact of food practices** into account, particularly in terms of sustainability, will be initiated together with the partners concerned. This highly integrative work will be expected to address a number of issues: societal (consumer expectations and behaviour, outlook for food in the face of climate change or health crises), nutritional (balanced diets), health (food safety, occupational exposure), environmental (sustainability of production and consumption methods, including home-grown food consumption), and even ethical (animal welfare, special diets, etc.).

[6] French poison control and monitoring centres

Such an integrative approach is strongly encouraged in the framework of the Horizon Europe calls for projects (cluster 6 "Food, Bioeconomy, Natural Resources, Agriculture and Environment") to which ANSES plans to respond.

THEME 4 – Participate in national, European and international exchanges and cooperative projects to fuel collective expert appraisals

Cooperation with ***Santé publique France*** – which covers a variety of topics such as foodborne illness outbreaks, PNNS, biomonitoring (particularly in the context of polluted sites and soils), PARC, etc. – is essential and will be strengthened, particularly to update epidemiological data on food-related topics relating, for example, to the issue of the share attributable to exposure in chronic diseases. This close interaction ensures synchronisation of the two agencies' missions and avoids redundancy.

ANSES's **National Reference Laboratories (NRLs)** will also seek to step up their **cooperation with the National Reference Centres (NRCs)**, particularly those in charge of activities on foodborne pathogens, with a convergence of surveillance databases including characterisation data and the associated metadata. Cooperation will be strengthened in investigations of clustered human cases of foodborne illnesses, or in the event of health crises due to contaminated food products. Research may also be carried out jointly in the spirit of the **One Health** approach.

ANSES will take care to maintain its **highly specific support for the public authorities** on **threats** (Biotox and Piratox plans). The agreements signed with major counterpart institutions (**CIRAD, CEA, Ifremer, Inserm and INRAE** in particular) will foster the development of joint research and the joint implementation of thesis projects.
A more general debate on areas for future research may draw on useful developments within the framework of the Aviesan and AllEnvi alliances.

At **the European and international level**, scientific exchanges (strains, sequences, contamination data, risk assessment models and methodologies, scientific personnel, etc.) will be promoted and targeted at partners with similar functions and with whom ANSES has forged regular and close relationships. Some of these have been formalised by **partnership agreements**: this is particularly the case in the European Union with the BfR, DTU-Food and RIVM, and soon with the ISS[7]. At the international level, partnership agreements have been signed with the US-FDA, CFIA, Health Canada, NIFDS and SFA[8], to allow exchanges and planning of joint projects.
A strategy of cooperation with French contributions in Europe and internationally may be established in the field of whole genome sequencing, within the framework of the Global Microbial Identifier (GMI) initiative, and following the international symposium organised jointly with the partners BfR, DTU-Food and NIFDS on the theme of "Foodborne Pathogens & Whole Genome Sequencing: Impact on Public Health Protection".

The ongoing collaboration with EFSA will contribute to research and risk assessment work, for example on nanomaterials as food additives or the assessment of food enzymes. This collaboration will be reinforced, with the support of ANSES as EFSA's National Focal Point, through funded projects already ongoing or others awaiting a response to calls for applications. Examples include the project on data collection, update and further development of biologically-based models for humans and animal species to support transparency in food and feed safety, coordinated by Wageningen Food Safety Research, and participation in the EFSA working group under the EURL for *Listeria* to establish a functional genome database. The terms for this enhanced collaboration will also be discussed as part of the debate on the establishment of **new partnership models with EFSA** in the context of the entry into force of Regulation (EU) 2019/1381 on the transparency and sustainability of the EU risk assessment in the food chain.

[7] BfR (Federal Institute for Risk Assessment, Germany), DTU-Food (Danish Technical University, National Food Institute), RIVM (National Institute for Public Health and the Environment, Netherlands), ISS (Italian National Institute of Health)
[8] FDA (Food and Drug Administration, United States), CFIA (Canadian Food Inspection Agency), NIFDS (National Institute of Food and Drug Safety Evaluation, South Korea), SFA (Singapore Food Agency)

Lastly, 2022 will see the continuation and finalisation of research carried out as part of various **pivotal European projects** and in particular the **One Health European Joint Programme (OH EJP)** coordinated by ANSES. The Agency's scientific teams are working on numerous OH EJP projects on **foodborne zoonoses, antimicrobial resistance and emerging risks**, as well as on cross-cutting integrative actions that will engage the Agency in a process of networking, exchanges of research equipment and scientific developments. The OH EJP is one of the first practical examples of the implementation of the One Health concept at European level.

Furthermore, ANSES will apply an active and dynamic approach to building and participating in **future partnerships under the Horizon Europe programme**. Indeed, the launch of this major seven-year programme (2021-2027) is a great opportunity to strengthen partnerships and cooperation. In December 2019, the European Commission proposed the European Green Deal to make the European Union's economy sustainable: boosting the efficient use of resources by moving to a clean and circular economy, in order to restore biodiversity and cut pollution.

In this context and in the framework of Horizon Europe, ANSES will be responsible for coordinating the **European Partnership for the Assessment of Risk from Chemicals** (PARC), with the definition of a strategic research and innovation agenda designed to facilitate the establishment of collaborative research programmes on surveillance and exposure, hazard characterisation, risk assessment, and the development of new scientific concepts and tools to address the challenges of chemical risk assessment.

In addition, other partnerships, which contribute to the EU's Farm to Fork Strategy for a healthier and more sustainable EU food system, a cornerstone of the European Green Deal, may be set up and are of major strategic interest to ANSES. These include the partnership on **Animal Health and Welfare**, in which ANSES has a particularly strong leadership role within the European working group tasked with preparing it, but also the one on antimicrobial resistance, in line with the **One Health** approach, and the one on **Safe and Sustainable Food Systems**; all these partnerships are currently being prepared.

Animal Health and Welfare - Animal Nutrition

Preamble

The details below present the main policy orientations proposed by ANSES in the area of **animal health, welfare and nutrition**. This section also reviews some of the major work completed by the Agency in 2021 and proposes a few key themes for the 2022 work programme of the Agency's laboratories, French Agency for Veterinary Medicinal Products (ANMV) and assessment departments with regard to animal health, welfare and nutrition.

Outlook for 2022

The coming year will be dominated by the consequences of the various health crises (COVID-19, avian influenza, TBEV, swine influenza, etc.) that have had a major impact on our 2020 - 2021 work programme. The laboratories have been particularly affected due to their necessary redeployment towards research and reference activities on these emergencies while maintaining the Agency's commitments to other activities. In the veterinary drug sector, 2022 will essentially be marked by the entry into force of Regulation 2019/6 on veterinary medicinal products and the continuation of its implementation in French law and within the ANMV.

A. Animal health research and risk assessment: new opportunities directly linked to health crises

The active involvement of our laboratory teams in the response to the COVID-19 pandemic, which was only possible due to the existing expertise on animal coronaviruses within our scientific community, has provided opportunities for new cooperative projects with French and international teams. Our scientists participated in the development of two calls for Priority Research Programmes and Equipment (PRPE) respectively on the PREZODE initiative to prevent emerging zoonoses and pandemics and on (Re)Emerging Infectious Diseases (EIDs), which have been validated by the ANR and on which our teams will be able to work. They will also contribute to several WHO programmes and a One Health EJP-funded project. Our expertise in tick-borne diseases, which enabled us to respond simultaneously to the emergence of TBEV in eastern France on the animal health and food safety fronts, also contributed to our integration into the IBEID LabEx with the *Institut Pasteur*. The efforts of our virologists, epidemiologists and Risk Assessment Department working on the re-emergence of highly pathogenic avian influenza H5N8 has generated questions that are already the subject of research and assessment work, which will be continued and expanded in 2022. Finally, for our laboratory teams, 2022 will be the year of a collective audit of research activities whose scope was defined in conjunction with our Scientific Board.

Risk assessment activities in animal health will target threats to France due to certain health hazards spreading across Europe. Even though the African swine fever epidemic among wild boars in Belgium was contained, this disease remains a huge threat and requires our preparedness. Since the numerous urgent formal requests conducted, our teams have also been maintaining a high level of readiness to assess any **risk of introduction** or spread of other urgent health hazards. Work on avian influenza, specifically to factor in the health data from the 2020-2021 epizootic, will move on to modelling so as to specify the impact of certain risk factors in order to better target risk management actions.

The results of the RESAVIP network's monitoring of influenza on pig farms have led authorities and professionals to consider the risks associated with human-pig interactions in the epidemiology of swine influenza viruses. A recent case of swine flu in a human in contact with a pig farm illustrated this problem, which will be addressed through a risk assessment project based on monitoring data and ongoing experiments at the Ploufragan-Plouzané-Niort Laboratory.

The question of the interface between **wildlife** and domestic animals recurs repeatedly in formal requests on animal health, requiring an **integrated approach** to risk assessment and calling on many complementary scientific disciplines in order to combine epidemiology, ecology and infectiology. The work of the **Vectors** mission (which was integrated into ANSES's activities in 2018) also leads to issues being addressed by taking simultaneous account of the health of humans, animals and the environment. This is how the Vectors expert group will respond to the formal request on the analysis of the risks for humans and animals associated with ticks of the genus *Hyalomma*.

These developments, which have been apparent for several years now, broaden the scope of such questions today, with the SARS-CoV-2 pandemic, which has an important One Health dimension. Incorporating this concept more systematically into the collective expert appraisal approach requires ANSES to pay close attention to interactions, not only between humans and animals, but also between humans, animals and the environment. The make-up of the expert groups whose animal health-welfare and nutrition mandates are to be renewed in 2022 will consequently be tailored accordingly.

The recent cluster of tick-borne encephalitis (TBE) that occurred in the Ain *département* following the consumption of unpasteurised cheese, investigated by the ANSES laboratories, led to a collective debate between the Biorisk and Animal Health and Welfare Expert Committees in order to set up a formal internal request to assess the risk of TBEV in France. This is likely to be a One Health type of request, taking into account human health, animal health and the role of ecosystems.

Applying this same One Health approach, the last of the four requests on botulism, which concerns wildlife, will call upon the Agency's vast potential for cross-cutting actions between its research, reference and risk assessment units in the fields of animal health and food safety, also taking into account the environment and wildlife.

B. Surveillance

Under the leadership of the Scientific Director for Epidemiology and Surveillance, along with the ESA Platform and its new coordination team, bee mortality monitoring will begin with the recruitment of a scientist at the PRADE joint technological unit hosted by our Sophia Antipolis Laboratory. This will enable the OMAA observatory for honey bee mortality and weakening to be started up again. Similarly, with the support of the DGAL and GDS France, the observatory for livestock mortality (OMAR) is expected to be consolidated in our Lyon Laboratory.

Along with its partners and through its strong commitment to coordination of the ESA Platform, ANSES will contribute to the effective functioning of a system that is vital to epidemiological surveillance of animal diseases in France. It will also guarantee complementarity with the risk assessment work required prior to the establishment of surveillance plans.

C. Analytical reference

Work in support of the DGAL by the teams at ANSES, GDS France and regional laboratories is expected to continue in 2022 and should in the short term lead to a strong regulatory framework for the **verification of reagents and diagnostic kits by the NRLs**. In particular, for each disease, this new framework will define the role played by the NRLs in the initial verification of diagnostic kits and in their possible batch-by-batch verification, and will enable a debate to be initiated on optimising the scheme in France and Europe. A debate initiated in 2021 on the frequency at which ILPTs should be organised has led to a more streamlined system, thus easing the burden on our partners from the participating departmental and private veterinary laboratories, while maintaining the same level of confidence in the quality of our network of first-line laboratories.

D. Antimicrobial resistance

We will continue our work on monitoring antibiotic use in animal production sectors and on antibiotic resistance of pathogenic and commensal bacteria, and our activities on this subject in 2022 will be marked by the end of EcoAntibio 2 and publication of the results from the research programmes funded by the EcoAntibio 2017 plan. With the help of the French Animal Health Network (RFSA), our teams will provide their partners with short videos presenting their main results on this topic. In addition, research activity in this area will be marked by the continuation of a programme on the detection of antibiotic use thresholds likely to trigger an excess selection of resistant bacteria. The Scientific Director for Antimicrobial Resistance will be responsible for implementing this plan and preparing new scheduling frameworks (Ecoantibio3, interministerial roadmap). There will be a particular emphasis on developing programmes to increase our knowledge of the mechanisms that support resistance.

The ANMV will continue its European work, in particular, on tools for monitoring the use of antimicrobials (ESVAC) and categorisation of antibiotics according to their importance for humans and the risks of transmission of antimicrobial resistance from animals to humans. This work is particularly important because it is used in the drafting and adoption of the delegated and implementing acts needed for implementing the regulation on veterinary medicinal products. The ANMV will continue its active participation in the working groups set up on this occasion, in particular chairing the group in charge of identifying antimicrobials whose use must be reserved for human medicine, and work on the European databases on the sale and use of antimicrobials. In the international arena, the ANMV will continue providing its expertise as an OIE Collaborating Centre for veterinary medicinal products, with a view to establishing the OIE's global database and conducting a debate on the management of quality records. On a national level, the ANMV will be pursuing its IT work to improve surveillance tools and their necessary adaptation to the various animal sectors (swine, veal, poultry and domestic carnivores). It will play an active role in the work of the Ministry of Agriculture to develop a database for declarations of sales of antibiotics. The database will collect retail sales data relating to practising veterinarians, pharmacists and companies producing medicated feedingstuffs. It will also participate in the steering committee for the Structural Reform Support Programme (SRSP) funded by the European Commission with the participation of the WHO to ensure the availability of older antibiotics and combat stock shortages.

Looking ahead to the revision of the interministerial roadmap for the control of antibiotic resistance and the Ecoantibio 3 plan to be developed, ANSES will contribute to the think-tanks set up. The Risk Assessment Department will in particular provide the DGAL with scientific information enabling it to specify measures to reduce the risk of spread of resistant bacteria (and/or the resistance genes they harbour) from animals to humans. The collective expert appraisal will focus on identifying a priority list of combinations of "bacterial species/resistance phenotypes" likely to be present in the animal sector and considered to be of public health concern, for which technical measures could be proposed, based on the available scientific knowledge.

E. Animal welfare

Reference work in the field of animal welfare took a decisive step forward in 2020 with the launch of the **European Union Reference Centre** (EURC) for the welfare of poultry and other small farmed animals, which ANSES has been tasked with coordinating with the support of Spanish, Italian and Danish research units. EURC activities in 2021 became fully operational despite constraints linked to the health crisis, notably conducting visits with Spanish teams to poultry slaughterhouses. The Centre’s activities will be ramped up in 2022.

ANSES's research and expert appraisal work on animal welfare relies on several Agency entities: a research unit within the Ploufragan/Plouzané/Niort Laboratory (EPISABE, from the merger of the EBEAC and EBEP units), a scientist within the PEBER Unit (Niort) of the same laboratory, the national animal welfare coordinator in the Strategy and Programmes Department, and the Risk Assessment Department (Unit for the assessment of food and animal health-related risks – UERSABA) together with the Expert Committee on Animal Health and Welfare (CES SABA) that it coordinates.

In the field of animal welfare assessment, given the public's interest in how animals live and die, and the importance that consumers would attach to a labelling scheme identifying animal rearing conditions, ANSES considered the relevant scientific basis on which various labelling approaches should be based and shared its thoughts with its Thematic Steering Committee on Animal Health. The Agency's experience in developing guidelines for professionals in a variety of fields has led it to take it upon itself to propose the definition of guidelines for the development of specific animal welfare labelling standards, based on its own definition of welfare.

F. European and international activities

At **European level**, within the framework of Horizon 2020, the coming year will see the continuation of the **One Health European Joint Programme (EJP)** coordinated by ANSES. The initial results of the research projects from its second internal call for projects are expected.

We should also mention the ongoing work for MOOD – MOnitoring Outbreak events for Disease surveillance in a data science context – a European animal health project coordinated by CIRAD in which ANSES is a partner, as well as the work of the five European research projects in which the Agency is participating (four of which it is coordinating) funded through the first call for projects of the ERA-NET on "International Coordination of Research on Infectious Animal Diseases" (ICRAD).

Meanwhile, the ANSES teams and scientists will continue their mobilisation and cooperation with EFSA on different work themes relating to animal health and welfare.

Cooperation and exchanges with European counterparts will continue in 2022 with, in particular, the strengthening of relations with the Friedrich Loeffler Federal Institute for Animal Health Research (FLI) in Germany, through the signature in late 2021 of a scientific cooperation agreement.

Moreover, besides responding to calls for European projects on specific themes, ANSES will pursue its efforts in 2022 on the design of a major Horizon Europe project for the creation of a European partnership on animal health and welfare. Similarly, our active participation in the work of the Joint Programming Initiative on Antimicrobial Resistance (JPI-AMR) and our future FAO Collaborating Centre on Antimicrobial Resistance deserve to be highlighted.

It should also be noted that within the framework of the French presidency of the European Union, PFUE 2022, various ANSES entities will be called upon to implement or contribute to actions and events, many of which will be carried out in conjunction with the French authorities and ANSES partners.

G. Outlook regarding veterinary medicinal products

The coming year will be marked by the implementation in January 2022 of Regulation (EU) 2019/6 on veterinary medicinal products. At European level, work on the adoption of the latest delegated and implementing acts and the development of new IT databases (including those for veterinary medicinal products and veterinary pharmacovigilance) must be finalised. A number of procedures and guidelines under the new regulation are also to be adopted by EMA with input from the national authorities competent in this area. In particular, the ANMV will continue managing the task force set up to prepare for the entry into force of the new regulation, which should assure further work in 2022. Similarly, at national level, major regulatory work remains to be finalised with the adoption of an ordinance and several decrees to adapt French law accordingly.

In the area of expert appraisals, the ANMV will finalise work in response to its internal request on risks associated with the use of external antiparasitics in the form of baths, showers and sprays for ruminants. The results of the internal request to assess the risks of herbal medicines in terms of consumer safety, completed in 2021, will be presented at a European symposium in the framework of PFUE 2022.
The further development of IT tools essential to the ANMV's activity and performance will also be a priority in order to ensure good interconnections between the European and national databases.

Lastly, the ANMV will resume as many of its **international activities** as possible, depending on the evolution of the COVID-19 health crisis. These involve in particular China, Saudi Arabia and Russia, in addition to its expert appraisal activities as a collaborating centre with the OIE, which specifically entails helping prepare the seventh cycle of training for national focal points.

H. Animal nutrition

In animal nutrition, work will continue on the various assessments relating to the European Commission’s easing of the feed ban. The ban, which followed on from the BSE crisis, applied to the vast majority of animal by-products used in the feed of food-producing animals. The improvement in the epidemiological situation has led the European legislator to propose alleviating measures.

On the regulatory front, 2022 will see the transfer to ANSES of a mandate to take decisions on the authorisation of tests on additives not yet permitted in animal feed.

Environmental health

Health and environment issues: what are the challenges facing ANSES?

Health and the environment are closely related. While some environmental risks to human health are known, and actions have been taken to mitigate their effects, the impact of many others has yet to be assessed in order to identify the associated health risks. These include the consequences of unsustainable consumption and the development of the circular economy, demographic changes and their territorial distribution (urbanisation and ageing of the population) and finally, industrial and technological developments that are not fully under control. Climate change, which has a major influence on the environment, ecosystems and biodiversity, is the priority issue for the coming years in terms of assessing the associated risks.

This assessment 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 either simultaneously or over successive periods of life, which are covered by the concept of the exposome, pose a major challenge to knowledge. Special attention should also be paid to agents potentially associated with serious or common diseases such as cancer and allergies, and health effects related to endocrine disruption. The various determinants of exposure must be clarified so as to identify levers for action able to control them.

Expert appraisal work and support for research on risks that have generated strong scientific and social controversy should continue to feature prominently in the Agency's activities. These include health risks associated with endocrine disruptors, nanomaterials and pesticides, as well as risks potentially associated with certain emerging technologies. Dialogue with the stakeholders involved in some of these themes will continue in forums, to fuel discussions on the Agency's work.

The environmental health actions to be developed over the next three years should take advantage of 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 optimised use of vigilance and research data.

Safety in terms of the environment and health will therefore be structured around several themes:

1. **Anticipate emerging threats and risks** associated with changes to the environment and climate that are sources of scientific and societal controversy;
2. **Improve/refine expert appraisal practices** to more effectively contribute to public decision-making, particularly by seeking to:
    - identify vulnerable populations and critical exposure situations (exposure windows, overexposure situations, etc.) including foetal/embryonic development and the first few years of life;
    - identify collective and individual uses and behaviours, socio-economic determinants that dictate the circumstances and modes of exposure, sources of social and environmental inequalities;
    - benefit from methodological progress in assessing levels of evidence and uncertainties for expert appraisal work.
3. **Develop the risk assessment tools** (cost-benefit studies, socio-economic studies, etc.) needed to ensure that risk management recommendations are better taken into account;
4. **Develop interdisciplinary methodological tools** to be able to assess 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;
5. **Support research in environmental health and consolidate synergies with expert appraisals**, 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. **Develop European and international collaborations** (participation in research consortia, strengthened bilateral relations with our counterparts, contribution to the work of international organisations such as the WHO, etc.).

Main challenges relating to chemicals

In line with various EU chemical regulation policies – in particular the EU chemicals strategy for sustainability adopted by the European Commission on 14 October 2020, which not only seeks to simplify the legal framework through a "one substance, one assessment" approach, but is also the first step towards the "zero pollution" goal for a toxic-free environment announced in the European Green Deal – the Agency will provide scientific input to the authorities through the following work.

- **Endocrine disruptors (EDs)**

In keeping with the Second National Endocrine Disruptor Strategy (SNPE2), signed at ANSES on 3 September 2020, the Agency is assessing substances with ED potential using a methodology for prioritising such substances published in 2021. The list of substances is defined on an annual basis following input from several Thematic Steering Committees (interCOT). The results are submitted at European level (European REACH and CLP Regulations, etc.).

As part of its assessments of plant protection and biocidal active substances (respectively under Regulation (EC) No 1107/2009 and Regulation (EU) No 528/2012), the Agency assesses the ED properties of all active substances for which it is the competent assessment authority. It is thus continuing to implement the "Guidance Document for the implementation of the hazard-based criteria to identify endocrine disruptors (EDs) in the context of Regulations (EC) No 1107/2009 and (EU) No 528/2012" adopted at European level.

- **Nanomaterials**

In a context of great uncertainty about the risks to human health and the environment associated with nanomaterials, the Agency's work in 2022 will aim to identify those that are both of little use and of significant risk. Referring to action 13 of the PNSE4, the aim of this work will be to describe the industrial sectors that use nanomaterials, based in particular on the use of data from the R-nano register that the Agency will continue to manage.

The Agency will continue to work on establishing reference values for nanomaterials – an action already undertaken for a specific form of TiO_2 – by requesting additional data from the reporters of these substances, in particular under the European REACH Regulation, and by analysing them.

- **Chemical mixtures and the exposome**

Building on its own work (Contalait project, irritants in indoor air, consumer products such as those for vaping, etc.), on European projects in which it is participating – including "Advancing Tools for Human Early Lifecourse Exposome Research and Translation" (ATHLETE), the follow-on from EUROMIX (in the form of a cooperation agreement) and the finalisation of HBM4EU on biosurveillance in Europe – and the international progress in this field, the Agency will be pursuing its activities through, in particular, the major European "Partnership for the Assessment of Risks from Chemicals" (PARC). The objective of this partnership is to develop the methodological foundations for ranking the priority chemical mixtures to be taken into account in its health-related expert appraisals. In line with this, the Agency will undertake to identify the methodological foundations for implementing the concept of the exposome in its work.

- **Health reference values (HRVs)**

Toxicity reference values (TRVs), indoor air quality guidelines (IAQGs), indoor dust guidelines, biomarkers of exposure (BMEs), occupational exposure limits (OELs) and biological values (such as biological limit values (BLVs) and biological reference values (BRVs) in the workplace) are all essential tools for both quantitative risk assessment and the definition, for example, of regulatory concentrations that should not be exceeded for health reasons. The Agency is strongly committed to the development of these tools. Work on them will focus on the needs related to industrial sites (classified installations for environmental protection – ICPE) and polluted sites and soil. Methodological work will be carried out on developing HRVs, mainly for chemical mixtures, in order to take advances in toxicology into account and better meet the challenges of health risk assessment. 2022 will be a key year for the revision of the Agency's methodological guide.

- **Assessment, classification and labelling of individual substances**

The use of chemicals is regulated within the European single market to ensure a high level of protection for European citizens and their environment. After 15 years of implementation and following adoption of the Chemicals Strategy for Sustainability, the REACH and CLP Regulations are slated for revision in 2022. The Agency will be involved in the preparatory work for these revisions in order to improve the health and environmental protection targeted by these regulations and to foresee their possible evolution. It will also continue its assessment of chemicals under the current regulations (those listed in the Community Rolling Action Plan (CORAP) and will re-assess those listed in past years, for which additional data have been obtained). There will also be an analysis of the best risk management options (RMOA), identification of substances of very high concern (SVHCs), proposals for restrictions on use when risk situations are identified, and a response to public consultations on revisions to methodological guides.

Under the CLP Regulation, the Agency will submit new proposals for the classification of chemical substances as needed.

The Agency will integrate in its expert appraisal work the components of the new European circular economy action plan, as well as the new EU policy (October 2020).

- **From the assessment of plant inputs to phytopharmacovigilance (PPV)**

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

With this in mind, the scientists involved in assessing these products have worked hard to develop or improve assessment methodologies. This work is most often undertaken in partnership with other organisations or as part of national, European or international working groups. Their purpose is not only to enhance the interpretation of assays used to determine chemical hazards, but also to construct detailed exposure scenarios and models used in assessing hypothetical risks and effectiveness. ANSES also funds specific studies to encourage the production of new knowledge needed for its expert appraisals.

The core purpose of PPV is to monitor the adverse effects of plant protection products (PPPs) on humans, plants, animals and more generally on all environments, and keep track of resistance. These actions will be strengthened to factor in biodiversity and the presence of PPP degradation products in the environment. Work will be directed towards the identification of substances of concern, mixtures and cumulative exposure. New strategic themes will be defined for the period 2022-2024.

- **Biocides**

Today, a minority of biocidal products have a marketing authorisation; most of these products are on the market without prior assessment. 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, the ambitious deadline for its completion having been set at 2024. The Agency is also very active in response to requests, and plays a key role in the assessment of applications for national and EU marketing authorisations for biocidal products.

In order to be able to assess the applications for which ANSES is responsible, those of its scientists involved in assessing biocidal products actively participate in the methodological developments carried out at European level, on issues that emerge as new product categories are evaluated.

➢ **Consumer goods**

The work carried out over the past few years on the assessment of risks associated with exposure to **consumer products** (play-mats or toys for children, textile clothing, nappies, feminine hygiene products, etc.) has highlighted the lack of knowledge on the chemical composition of many products, the presence of undesirable contaminants (skin sensitisers, carcinogens, etc.) in some of them, and more generally raises questions on the safety of numerous products. In the new French legislative context resulting from the AGEC Act (against waste and for the circular economy), the Agency will focus on identifying new uses for recycled products. It will also remain active in the area of the environmental dispersion of plastics in different matrices and their reuse and consequences in terms of health effects.

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), the assessment of the risks associated with their consumption is hampered by the complexity of the mixtures, the variability of emissions during the combustion or aerosolisation processes in keeping with the variety of materials and consumption practices, and the partial documentation of the hazards associated with the inhalation of the ingredients and additives they contain. After completing in 2020-2021 a review of the products declared in support of regulatory action, categorising the substances and better defining the behaviour of vapers, the Agency will begin in 2022 to assess the risks relating to vaping products that offer an opportunity to quit smoking.

➢ **European and international work on chemicals**

ANSES, which participates in numerous European projects, will also cooperate in the 2nd European Joint Action on Tobacco Control 2 (JATC 2) to support the Tobacco Directive. As in previous years, ANSES will continue to participate in the WHO's Chemical Risk Assessment Network (WHO/IPCS), whose objective is to improve chemical risk assessment by promoting interactions between organisations. If the proposal submitted in autumn 2021 for the PARC partnership is accepted for funding by the EC under Horizon Europe, from its inception in 2022 ANSES will be in charge of both its overall scientific and administrative coordination, and of leading and playing a key scientific role in several of the programme's work areas. This partnership is designed to provide chemical risk assessors and risk managers with new data, knowledge and methods. It will also develop the network of specialist players and the scientific skills required to address current, emerging and new challenges in chemical safety.

Main challenges relating to water

The EU's project to revise Directive 98/83/EC on the quality of water intended for human consumption led to the publication of the new directive at the end of December 2020 and its entry into force on 12 January 2021. It is the European regulatory framework for drinking water. EU Member States have two years to transpose the provisions of this directive into national law. ANSES and its expert groups will therefore be actively involved in examining some twenty draft texts between now and the summer of 2022.

These texts, which are the future regulatory framework for the quality of drinking water, from the resource to the consumer's tap, will notably lead to a redefinition of the way ANSES works at French and European levels on materials in contact with water. They also raise multiple questions about the assessment of past or emerging risks related to regulated, non-regulated, or recently-regulated chemical contaminants that may be present in water resources and more generally in aquatic environments, such as nanoparticles, microplastics, drug, cosmetic and pesticide residues and metabolites, as well as the issue of the effects of mixtures.

All these activities should be placed in the context of the impact of climate change on the various environmental media (particularly water stress), a particularly sensitive subject with regard to water resources (availability of the water resource, modification of its characteristics, etc.), the need to preserve this resource, and questions about the effectiveness and safety of wastewater reuse systems, for which proposed new uses are proliferating within the framework of the France Experimentation and AGEC Acts.

Other issues on which the Agency will focus its action concern both inland and coastal recreational waters, in particular the question of biotoxin producers, some of which affected the health of bathers, surfers, professionals, etc. exposed to contaminated spray this summer along part of the French coastline. With regard to swimming pool water, in addition to the Agency's permanent mission relating to the assessment of the safety and efficacy of treatment products and processes, Act No. 2020-1525 of 7 December 2020 on the acceleration and simplification of public action (ASAP) transferred to ANSES, as of 1 March 2021, the decision to authorise the water treatment products and processes mentioned in Article L. 1332-8 of the French Public Health Code, making it possible to meet the quality requirements for swimming pool water. In this context, ANSES will undertake the updating of the guidelines (ANSES, 2011) listing the documents required to compile marketing authorisation applications for swimming pool water treatment products and processes.

Main challenges relating to air

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

Among the main issues that the Agency will have to address are mixtures of substances in the air, including pesticides, the duality of scientific and regulatory guidelines for characterising exposure to particles/aerosols for the general population and workers, emerging non-regulated pollutants (such as carbonaceous compounds in particles and ultra-fine particles) as well as settled dust in indoor and outdoor air (risk assessment, proposed guideline values, etc.).

As part of the strengthening of European legislation on ambient air quality, announced by the European Commission for 2022 (possible revision of Directives 2008/50/EC and 2004/107/EC), and following publication of the updated WHO guideline values in September 2021, the Agency will continue its action to support public authorities in defining new standards and regulatory thresholds.

Regarding indoor air, ANSES assesses the risks related to pollutants present in different types of indoor environments (establishments open to the public, homes, etc.) where certain characteristics (size, presence of ventilation/aeration, frequency of use, equipment and/or furniture present, user practices, etc.) have an impact on indoor air quality.

Health effects associated with biological agents or bio-aerosols (mould, toxins, pollen, viruses) are increasingly well known (allergies, infections, etc.). The foreseeable developments due to climate change concerning the presence of some of these agents in the air justify an assessment of medium-term health risks and the potential economic impact they may have. On the subject of SARS-COV-2, ANSES's work will enable the public authorities to implement proportionate prevention and management actions.

The Agency's work will focus on situations involving the populations most at risk (particularly in relation to workplace exposure) and/or most vulnerable due to particular sensitivities, or socio-economic determinants that are sources of social and environmental inequalities. It will also require efforts to develop air contamination assessment studies and improve the accessibility of their findings for expert appraisals and research.

Main challenges relating to physical agents

The development of technological innovations is often associated with their rapid spread across all economic and social activities. The Agency therefore needs to maintain its monitoring activities on the impacts of these new technologies, whose uses are constantly changing.

As innovative digital communication technologies constitute a new source of individual and collective exposure to electromagnetic fields, their use raises both questions about their possible effects, and scientific and societal controversies on the subject, justifying the Agency's actions. ANSES has risen to the challenge of documenting the ways in which these technologies are used and assessing the corresponding exposure, along with potential health effects. This issue is particularly important in the context of the deployment of 5G.

Expert appraisals to update knowledge on the possible links between RF exposure and cancer will continue throughout the coming year. The Agency will also continue to support the Cosmos-France study run by the International Agency for Research on Cancer (IARC), as part of the French contribution to the creation of a large cohort in order to collect data on exposure of the population to electromagnetic waves and on their health.

In addition to the effects of electromagnetic fields on health, the use of digital technologies can have other health effects, especially by modifying behaviour (leading to, for example cognitive disorders, addictions, a sedentary lifestyle, accidents, etc.). In 2022, the Agency will continue the expert appraisals already initiated to assess these effects and their determinants on the physical and mental health of children and adolescents.

With regard to noise pollution, the social cost of which is considerable in France, the extra-auditory effects of noise are increasingly well known (sleep, cardiovascular, cognitive and school learning disorders, etc.). Its impact nonetheless remains to be fully characterised. While looking ahead to an assessment of the health impacts of noise pollution that will take into account specific territorial characteristics (typology of housing and its changes, social environment, etc.) and, if possible, of the potential impact of global warming with particular reference to the management of doors and windows, the Agency will continue to monitor changes in sources and modes of exposure to noise. As part of the PNSE4 actions to reduce exposure to noise, and in a context of strong social and environmental inequalities, the Agency will initiate a debate on how to assess the health benefit that can be derived from the implementation of noise reduction/attenuation measures, in particular for the most exposed populations.

In addition to ANSES's work on the impact of noise on human health, the effects of noise on biodiversity should be the subject of particular attention using a holistic approach.

Main challenges relating to vectors

Given the spatio-temporal extension of insect vectors of pathogens for humans, animals and plants, the Agency will actively pursue the vector control actions already initiated. In 2022, the Agency will finalise its method for assessing vector control strategies in order to implement it in various territories. Given the small number of biocidal solutions on the market, ANSES will pay particular attention to the effectiveness of alternative methods and remain vigilant with regard to the rise in resistance.

Continued support for research through the National Research Programme for Environmental and Occupational Health (PNR EST) is essential in order to produce the knowledge needed for the Agency's risk assessments in the area of vector control.

Plant health and protection

France's agricultural, forestry, ornamental and environmental plant health situation is affected more and more by the consequences of the increased frequency and volume of world trade in plant products, the impacts of global climate change, and changes in farming practices and crop management techniques. Greater 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 the 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 of these factors 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 also possesses considerable overseas territories, which are ecologically fragile and particularly exposed.

Plant health and protection topics are handled at ANSES by two research and reference laboratories (the Plant Health Laboratory and the Lyon Laboratory), two risk assessment departments (the Risk Assessment Department – DER, and the Regulated Products Assessment Department – DEPR) and by the Market Authorisations Department (DAMM).

The Plant Health Laboratory (LSV) brings together a number of different thematic and technical units: bacteriology, virology, genetically modified organisms (GMOs), entomology & invasive plants, mycology, nematology, quarantine, pests & tropical pathogens. It carries out reference missions as the National Reference Laboratory (NRL) and has three European Union Reference Laboratory (EURL) mandates. It also conducts research in plant health, in particular on regulated or emerging plant pathogens and pests, invasive plants, and detection of GMOs. Lastly, it provides support for surveillance.

The Lyon Laboratory studies the emergence and development of resistance to PPPs in plant pest populations through its Contracted Unit for Characterisation and Monitoring of Phenomena of Pesticide Resistance Development (CASPER USC) in partnership with INRAE. In addition, the work of its Unit for Epidemiology and Support for Surveillance (EAS Unit) includes providing assistance with the development of epidemiology activities and contributing to national surveillance in the area of plants.

With regard to the departments involved in expert appraisals for risk assessment, **the DER (part of the Science for Expertise Division)**, whose scope encompasses the work of the Expert Committee (CES) on "Biological Risks for plant health", receives scientific and technical support from the LSV. The Phytopharmacovigilance and Observatory of Pesticide Residues Unit (UPO) manages a scheme for detecting and monitoring resistance and the adverse effects of PPPs on human health, fauna, flora and the environment (phytopharmacovigilance).

It should be noted that with effect from 2022, the DER will also work on all risks associated with the release of GMOs, some of which are used in control measures to protect plants.

The DEPR assesses the hazards and risks to humans, animals or the environment, as well as the agronomic benefits, of several families of **regulated products**: plant protection products and substances, fertilisers and growing media, and non-indigenous macro-organisms beneficial to plants that are introduced into the environment, in accordance with European and national regulations. It relies on the skills within the CES on "Plant protection substances and products, biocontrol", the CES on "Fertilisers and growing media" and the Working Group on "Macro-organisms beneficial to plants".

Lastly, **the DAMM** is responsible for marketing authorisations and permits (for parallel trade and experimentation) relating to PPPs, fertilisers, growing media and their adjuvants. It receives the application dossiers and reviews the draft decisions. It also manages declarations of product testing and experimentation, the operation of the Marketing Authorisations Monitoring Committee, and product control and inspection activities.

The Agency therefore adopts a comprehensive approach to plant health and protection by studying the interactions between plants, pathogens and pests, and the regulated products used, while taking all the health, economic and societal aspects into account.

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

A. Main outlook in plant health and protection

➢ Plant health: from risk assessment to national surveillance

In late 2021, six pests were the focus of particular attention in the French plant health landscape: the bacterium *Xylella fastidiosa*; the bacterium responsible for yellow dragon disease also known as huanglongbing (HLB); the pinewood nematode; tomato brown rugose fruit virus (ToBRFV); the fungus *Fusarium oxysporum* f.sp. *cubense* race 4 (Foc TR4) responsible for Panama disease in banana crops; and the oriental fruit fly *Bactrocera dorsalis*.

Assessment, ranking and anticipation of risks

The LSV's Expert Assessment of Biological Risks (ERB) Unit, which reports functionally to the DER, was asked to investigate a variety of issues covering France's overseas territories (specifications relating to the obligations of establishments producing *in vitro* banana plants for Guadeloupe, French Guiana, Martinique, Mayotte and Reunion Island, and the conditions for acclimatising these vitroplants in these same territories) as well as metropolitan France (express risk assessment of *Popillia japonica*, the Japanese beetle, and control strategies for canker stain of plane trees, *Ceratocystis platani*). It is also working in fields at the crossroads between plant health and human health, with the analysis of data from poison control centres on exposure to caterpillars that shed stinging hairs, an analysis of the health risks associated with exposure to these caterpillars, and the formulation of management recommendations. These problems concern woody species in forests (caterpillars with stinging hairs such as the pine processionary caterpillar *Thaumetopoea pityocampa,* the oak processionary caterpillar *Thaumetopoea processionea,* or the browntail moth caterpillar *Euproctis chrysorrhoea*, for hazelnut, beech or oak in particular), fruit trees, ornamental trees and crop plants. In addition to the usual aspects, this work will include an analysis of the joint risk to humans and biodiversity.

In line with the increased need for vigilance, ANSES's assessment mission also uses a new approach to pre-empting emerging risks, through continuation of the EFSA-funded European programme Horizon Scanning for Plant Health. This monitors the media and scientific literature in order to identify new plant pests by finding relevant information on pests that could become a cause of concern for the countries of the European Union.

Reference: integrating technological developments while preserving skills that have become rare

The reference mission will remain the LSV's central activity. To continue to respond promptly in 2022 to needs regarding biological monitoring of the country, including for emerging threats, and provide identification services to the agricultural sector more broadly, the LSV will:

- propose in-house or tailored methods;
- characterise them according to standards defined at the Agency (method validation guide) or at European level (EPPO);

- improve existing analytical methods by integrating technological innovations where necessary, particularly molecular innovations (NGS[9] and third-generation sequencing, metabarcoding), to improve their performance (e.g. on new complex matrices) while optimising their cost;
- support the transfer of these methods to approved laboratories as necessary. The corresponding methodological support could include kit validation.

However, analytical methods and identification tools using classical morphological or morphobiometric techniques (more specifically in nematology, entomology and botany) will be promoted because:

- they have become rare in the national and European scientific landscape;
- in a more generic integrative taxonomy approach, they enable the validation in molecular databases of pest sequences derived from the flow of interceptions or entries.

In general, the LSV works to maintain a high level of taxonomy skills for its reference mission. It will confirm its ability to organise inter-laboratory tests (ILTs) by continuing their international implementation, and to monitor the network of approved French laboratories under the ISO/CEI 17043 standard.

In Europe, this period will see the promotion of the Horizon 2020 VALITEST[10] project, coordinated by the LSV's Reference Coordination Unit (UCR), which produced validation data through two series of diagnostic test validation studies including different combinations of pests/plants/matrices.

In addition, 2022 will see our activities expanded to include knowledge dissemination and technical training, within the framework of EURL mandates for fungi & oomycota, insects & mites, and plant-parasitic nematodes.

Research: gaining visibility

To maintain its analytical capacity at a high level, the LSV will also get involved in research and development programmes that will provide the reference mission with new knowledge and innovations.

To achieve this, the research questions addressed in responses to calls for tenders for national (ANR, Ecophyto, regional programmes), European and international (ERA-NET EUPHRESCO) collaborative projects will mainly concern:

- the biological characterisation and phylogeny of emerging pests or those considered to pose a risk;
- the study by molecular typing (MLSA, MLST) or sequencing (metabarcoding, WGS) of the genetic diversity, structure and adaptive potential of populations of these organisms;
- any vectors of these pests and their geographical distribution.

In addition, the LSV will develop its participation in the study of regulated and emerging pest dispersion, for example by improving sampling techniques, characterising biological cycles and identifying factors determining the success of introduction and establishment.

New structural and visible links with our academic partners will be expanded: in addition to the one formed with INRAE and the DGAL via the Pesticide Resistance Forum and Research (R4P) network, there is the NemAlliance cluster (mycology contracted unit with INRAE) and the DIAGEPITROP partnership with CIRAD.

[9] Next-generation sequencing
[10] VALITEST – Validation of diagnostic tests to support plant health (May 2018-October 2021)

Surveillance: contribution to surveillance schemes and active participation in the epidemiological surveillance platform for plant health

This concerns:

- national surveillance plans drawn up by the Ministry of Agriculture;
- epidemiological monitoring carried out as part of projects with the production sectors;
- its contribution to the epidemiological surveillance platform for plant health (ESV) in conjunction with the Lyon Laboratory's EAS Unit. To kick off its activities, this platform will be aiming to improve official surveillance schemes, develop health reports based on surveillance data, establish monitoring of plant health hazards and improve the quality of surveillance data and international health monitoring. In addition to these cross-cutting themes, several working groups are looking to improve the surveillance of specific plant pathogens: *flavescense dorée* and vine wood diseases, the polyphagous bacterium *Xylella fastidiosa*, huanglongbing and the pinewood nematode. The Lyon Laboratory's EAS Unit will be involved in the cross-cutting support for this platform, meaning that ANSES will participate in its coordination;
- coordination of the LSV's in-house Working Group on "Epidemiology in plant health".

Its most significant activities for the period 2020-22 include:

- validation by the laboratories of updated or innovative analytical methods for identifying and characterising regulated or emerging pests;
- joint coordination of the epidemiological surveillance platform for plant health (ESV) by the Lyon Laboratory's EAS Unit;
- participation in and/or facilitation of the platform's working groups by laboratories, as well as other Agency entities, in order to improve the specific surveillance schemes and provide cross-cutting expertise in surveillance engineering;
- research conducted to improve surveillance;
- expert opinions on the basis of formal requests in order to define certain surveillance plans via ad hoc recommendations.

This surveillance mission is also intended to evolve and innovate in terms of both methods and research questions. It will draw on the existing networks involved in plant health organisation (sectors, interprofessional organisations, FREDON and FDGDON, etc.) in order to alert the official services to the development of risks in the different geographical areas: metropolitan France, EU Mediterranean countries, French overseas territories.

Overall, expanding plant health missions and an evolving context

The scope of the LSV's activities will also be impacted by the introduction of new standards such as the new version of ISO/CEI 17025, and new European regulations, which (i) have resulted in the French overseas territories being regarded as third countries in relation to the EU from the end of 2019, (ii) concern the setting up of the three EURL mandates mentioned above for official controls on plants and their health status via Regulation (EU) 2017/625, and (iii) will result in Regulation (EU) 2016/2031 being applied within the framework of the new Plant Health Act. The coming years will provide room for debate and the corresponding actions, in terms of acquiring skills to match the new regulatory demands.

➢Plant protection: from the assessment of plant inputs to phytopharmacovigilance

Continual improvement in assessment methodologies for plant inputs

The challenges identified for the coming years in assessing plant inputs, both for synthetic PPPs and biocontrol products, lie in the production of knowledge and methods to ensure that a high level of protection of 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 involved in assessing PPPs, fertilisers and growing media are participating in numerous studies to develop or optimise assessment methodologies, particularly with regard to cumulative or "cocktail" effects. This work is most often undertaken in partnership with other organisations or in the framework of national, European or international working groups. Its purpose is not only to enhance the interpretation of assays used to determine chemical hazards, but also to construct detailed exposure scenarios and models used in assessing hypothetical risks and agricultural benefits (taking into account the resistance phenomena that have been identified or are liable to develop – see the section on phytopharmacovigilance). ANSES also funds specific studies to encourage the production of new knowledge needed for its expert appraisals.

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 should 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 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 introduction into the environment. The DEPR will remain in charge of examining applications for the importation into France of macro-organisms for use in non-contained conditions. **A methodological guide specifying the information to be provided in applications for the release into the environment of non-indigenous macro-organisms beneficial to plants will be developed, in order to facilitate the submission and assessment of such applications.**

Issuing of MAs: facilitate the submission of applications, optimise their processing and provide easier access to information

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

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 scope of authorisations, 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 was rolled out for a limited number of applicants and is now being deployed for all companies. It allows them to enter the information required for their applications to be examined.

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 on plant protection products and fertilisers will also be made available on the website. Changes are also planned to the E-Phy site and to open data, the catalogue of products and their conditions of use, as well as the management of rapid, personalised responses to requests made on the site.

The MA Monitoring Committee, whose members will be renewed, will continue to support the General Directorate, particularly with regard to the management measures proposed in the decisions.

The department will continue work on the comparative assessment of products containing substances that are candidates for substitution. In this context, a key issue is the assessment of applications to renew MAs for products containing copper.

Characterisation and monitoring of resistance: aiming for more upstream anticipation through new technologies and more downstream integration in the agricultural and economic landscapes

The task of the Lyon Laboratory's CASPER USC is to study emerging resistance phenomena in the main plant pests (fungi, insects, bacteria, weeds) to plant protection products. It helps establish and implement the DGAL's surveillance plans concerning the "Resistance" component of the monitoring of unintended effects of plant protection products. It provides its expertise to risk assessors (examination of dossiers for the DEPR) and managers (participation in the drafting of joint technical notes on "Resistance" with the DGAL, INRAE and technical institutes). Its research on the mechanisms involved in resistance phenomena is mainly carried out with the partners of the four INRAE units specialising in this field from the Pesticide Resistance Forum and Research (R4P) network.

In a context where there are calls for a reduction in the number and diversity of authorised active substances, resistance of pests and diseases to plant protection products becomes a key issue: each treatment must be as effective as possible and its use reasoned in order to limit the evolutionary response of the target organisms. With this in mind, the Unit develops methods and tools for detecting resistance through both biological and molecular approaches. The scientific orientations of the CASPER USC for the period 2021-2022 will be:

- monitoring of emerging topics in relation to feedback from the field and in conjunction with the DGAL as part of the annual PPP resistance surveillance plan. The USC and the R4P are both involved in creating and updating a database of cases of PPP resistance in France. This work is also being carried out at the European level through EPPO;
- adaptation of high-throughput sequencing methods for more accurate surveillance and monitoring of the development of resistance phenomena in pest populations;
- assessment of the cost (or lack thereof) of resistance in pest populations. This parameter is essential in terms of understanding and managing resistance phenomena in the field;
- study of the effects of landscape and cropping practices on changes in the occurrence and frequency of resistance in pest populations.

The work carried out in this surveillance mission may also benefit the phytopharmacovigilance mission (PPV, see below) by identifying the emergence of resistance to PPPs in pest populations.

Phytopharmacovigilance: collect and analyse data, identify the health or environmental signals

Created under the French Act on the future of agriculture, food and forests, the purpose of the phytopharmacovigilance (PPV) scheme is to collect data on adverse effects occurring following the use of PPPs and identify any health or environmental signals among these data. The scheme's scope covers effects on humans, livestock animals including honeybees, cultivated plants, biodiversity, wildlife, water and soil, air quality and food. 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 and its supervisory ministries.

The main source of information reporting is the network of partner surveillance and vigilance schemes. Some twenty partners regularly forward surveillance or vigilance data on adverse effects of PPPs. This network's contribution is supplemented by reports that can be sent directly to ANSES via a reporting portal on the Agency's website. Lastly, the scientific literature, along with the technical literature and the press, are another complementary source of information. These sources do not all yet fully meet the expectations of the PPV scheme, so efforts are needed to improve this.

Once the data have been collected or sent to ANSES, they are analysed to single out those regarded as health or environmental signals, on the basis of criteria relating to the severity of the effect, its causality regarding PPPs, and the risk of the effect's recurrence. ANSES still needs to consolidate the signal identification processes.

Lastly, ANSES can initiate ad hoc studies on the adverse effects of PPPs when the information is incomplete or to further examine a report on an adverse effect. In contrast to more open research questions, these studies should help answer specific questions and produce results that can be used quickly, for example to adapt the conditions of an MA or define cross-cutting management measures. These studies are funded through a tax paid to ANSES by MA holders on the revenue from sales of PPPs.

For the period 2019-2021, the Agency adopted a strategy for phytopharmacovigilance, broken down into four areas, which provides overall guidance for its work:

1/ Collect signals: focus on increasing the number of relevant signals provided by the network of partners that contribute to PPV;

2/ Consolidate signal characterisation and processing, and supplement these processes with the detection of emerging phenomena;

3/ Formulate summaries and recommendations on completion of the PPV analyses, and ensure they are adopted by all stakeholders;

4/ Continue consolidating the "Studies" component of PPV through implementation of the priority themes defined for the period 2018-2020:

- exposure of the general population to PPPs, particularly via ambient air, and of specifically exposed populations, for example residents in cultivated areas;
- exposure of agricultural workers to PPPs;
- the presence of PPPs in soil and the effects of PPPs on biodiversity;
- the effects of PPPs on bees and other pollinators.

5/ Enhance the "Reporting" of PPV actions to all stakeholders in France and encourage the emergence of similar mechanisms at European or international level.

The coming year will be an opportunity to set out the new challenges of the vigilance strategy for the period 2022-2024.

Occupational health

Occupational health has regularly been in the spotlight over the past two years, mainly due to the COVID crisis and the recent Act of 2 August 2021 to strengthen occupational health prevention, but also because of publication of the report from the Third National Occupational Health Plan (PST3) for 2016-2020 and preparation of the next PST for the period 2021-2025.

In June 2021, the European Commission published the strategic framework that will guide its policy on health and safety at work for the period 2021-2027. This focuses on three main priorities, which will undoubtedly be echoed in the PST4:

- anticipating and managing change in the context of green, digital and demographic transitions;
- improving the prevention of work-related accidents and diseases, and striving towards a Vision Zero approach to work-related deaths;
- increasing preparedness to respond to current and future health crises.

This is the context for the orientations presented below, which the Agency intends to implement from 2022 on the theme of occupational health, accompanied by various actions that will be initiated or completed at the same time.

These actions are fully in line with the principles of ANSES's goals and performance contract (COP, 2018-2022).

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

The detection of emerging or re-emerging occupational health risks is one of the Agency's fundamental missions that relies on monitoring, research and vigilance work.

Thus, while pursuing its routine work to produce data and knowledge to support expert appraisal or develop tools for detecting emerging cases of new occupational diseases, in 2022 the RNV3P[11] will continue its discussions on optimising the scheme, taking better account of environmental diseases, and developing the occupational exposure thesaurus.

On this last point, within the framework of the PST4, ANSES will continue coordinating work on the evolution and harmonisation of the occupational exposure thesaurus, together with the network's partners and occupational health stakeholders, with the aim of improving the interoperability of databases, particularly those set up and maintained routinely by occupational health services for their own needs.

ANSES also manages or leads other vigilance schemes, such as toxicovigilance, veterinary pharmacovigilance and phytopharmacovigilance, whose functions and collection methods differ but which are also used to identify emerging adverse effects or health problems related to work. The vigilance data they generate provide regular exposure information and reports of cases to supplement and extend risk assessments.

In accordance with the COP, work will continue in 2022 to ensure the consistency and coordination of these vigilance schemes. It will strengthen and improve each scheme's effectiveness in identifying relevant signals, particularly regarding the detection of emerging occupational diseases.

[11] RNV3P: National Network for the Monitoring and Prevention of Occupational Diseases.

Mobilise multidisciplinary scientific expertise to support French and European public policies and decision-making

The production of knowledge on hazards and exposure, as well as the assessment of health risks, are central to the Agency's activities and expertise, especially in the field of occupational health. Much of this work concerns chemicals and is also related to implementation of French public policy actions (PST4, PNSE4, SNPE, etc.) or decisions taken within the framework of EU or national regulations on the assessment and management of chemical risks. As part of these permanent missions, ANSES will continue to provide reference support with expert appraisals conducted for European regulations **(CLP, REACH, Plant protection products, Biocides, Fertilisers, Veterinary medicinal products)**. Most of these regulations include a component on occupational exposure and risks.

One of the Agency's major challenges regarding risks to workers is to identify substances to be assessed as a priority, in order to maximise the impact in terms of prevention and protection. European work on exposure assessment and changes in technical standards due to advances in scientific knowledge will be monitored to ensure overall consistency and harmonisation of practices among the various regulations. This will be facilitated by the diversity of regulatory fields within the Agency's missions. Looking ahead to the PST4, the aim is to leverage the expertise produced within this framework for improving information, occupational risk prevention and health protection in the workplace.

All the expert appraisal work mentioned will pay particular attention to endocrine disruptor (ED) and carcinogenic, mutagenic, or toxic for reproduction (CMR) substances, in order to improve knowledge of hazards and exposure, including occupational exposure, on these substances and while providing French expertise at the European level so that suitable management measures can be taken where necessary.

Besides a substance-by-substance approach, the goal and major challenge for the Agency will be to maintain efforts already under way to develop new knowledge and robust methodologies to take the combined effects of chemical mixtures into account. More broadly, the Agency will strengthen its ability to work in a multidisciplinary way and to integrate its various fields of expertise around the concept of the exposome.

It is important to emphasise that many French and European workers are still exposed to CMR substances that "evade" European risk management systems such as REACH or CLP. This mainly concerns exposure to carcinogens from work or industrial processes, which are not intended to be marketed, such as diesel emissions or crystalline silica dust. For this reason, the Agency was asked by the Ministry of Labour to do two things: 1/ propose a method for concluding whether a **process is carcinogenic** and define classification criteria to justify a process's inclusion in the ministerial order laying down the list of carcinogenic substances, preparations and processes within the meaning of the French Labour Code, and 2/ analyse several processes with a view to their inclusion in the ministerial order. After publishing its expert appraisal on cytotoxic and cytostatic substances in 2021, the Agency will publish its work on welding fumes in 2022, before defining classification criteria to justify a process's inclusion in the ministerial order and proposing a method for concluding whether a process is carcinogenic. This work could also serve as a basis for dialogue for the Ministry of Labour in the European discussions on amending Annex I of Directive 2004/37/EC establishing the European list of carcinogenic substances, preparations and processes.

As part of the implementation of the memorandum of understanding with the DGT specifying the signatories' role and tasks in implementing the work programme on **occupational exposure limits (OELs)**, the Agency will continue its scientific expert appraisal work with a view to making recommendations for atmospheric **OELs** and biological limit values **(BLVs)**, as well as its contribution to European work on OEL recommendations led by ECHA[12]. The aim is to identify the substances to be assessed as a priority in order to optimise the impact of the expert appraisals conducted in terms of risk protection and prevention. Furthermore, in the coming years, it will be necessary to increase ANSES's ability to develop biological limit values, which will help in particular overcome the uncertainties associated with the

[12] ECHA: European Chemicals Agency

inhalation exposure route alone, as well as the number of OELs concerning nanoparticle substances, in accordance with the objectives mentioned in the PST4 currently being finalised.

After having first conducted a review of knowledge on current analytical methods for determining the main characterisation parameters of nanomaterials, ANSES provided support to its supervisory ministries in 2021 for responding to the public consultation issued by the European Commission with a view to proposing a new definition of nanomaterials. In 2022, ANSES will continue its deliberations on the question of this definition, and will publish an opinion that includes not only its response to the Commission from the consultation and an analysis of the relevance of parameters and thresholds (e.g. size, percentage in number of particles, etc.), but also a problem-oriented analysis of the broader context of regulating nanomaterials and related controversies. In addition, an assessment of the annual declaration scheme for nanoparticle substances (R-Nano) and its ability to serve the various objectives of traceability, public information and health risk assessment was published in late 2020. A number of recommendations were made to consolidate the register, improve the quality of the data it contains, and improve knowledge about these substances. The establishment of a multidisciplinary working group to support the R-Nano register will help with consolidation of the declared data, as well as their exploitation, which is still currently limited. In conjunction with the actions of the National Environment & Health Action Plan (PNSE4) and the National Occupational Health Plan (PST4) on the safety of nanomaterials, this data exploitation should focus on the identification and analysis of emerging signals (new sectors, high-tonnage substances, etc.), a precise description of substances found on the market, and documentation of nanomaterials within certain industrial sectors and the resulting potential exposure, particularly occupational exposure.

Following on from its expert appraisals on the identification and assessment of CMR substances and its most recent work to assess the benefits of formaldehyde regarding its use in certain industry sectors (pathological anatomy and cytology, embalming, etc.), the Agency will continue to work on assessing substitution products and processes according to the formal requests it receives. In a study published in 2021[13], ECHA reported on the effectiveness of the REACH authorisation procedure, and especially how it incentivises substitution. In particular, it found that during the review phase of authorisations already issued, when new applications had to be submitted before expiry of the authorisation, the volume of substances concerned by the various applications dropped by 97%, from 19,000 tonnes per year to 600 tonnes per year. Another study conducted by the European agency[14] reported that manufacturers themselves seemed to recognise the value of the authorisation procedure, as it was for them the main trigger for starting a substitution process. Based on these observations, priority will be given to participation in European initiatives to promote substitution through ANSES's contribution, for example, to the procedure for identifying SVHCs[15]. The Agency will also address occupational health issues in the context of preparatory work for the revisions of the REACH and CLP Regulations, planned for 2022.

Lastly, in the context of its new mission relating to **expert appraisals prior to creating or modifying occupational disease tables** or recommendations to the CRRMPs[16], the Agency published its first founding report in October 2020. Indeed, the development and publication of a methodology as a basis for the Agency's expert appraisals in response to formal requests was an essential prerequisite for the successful launch of this new mission.

ANSES then followed this in late 2020 with the completion of its first long-awaited expert appraisal report on the link between pesticides (including chlordecone) and prostate cancer. In 2021 this was presented to the occupational disease commissions for the general health scheme (CS4 of the COCT[17]) and the agricultural scheme (COSMAP[18]). Within the framework of this mission, ANSES's work programme includes finalisation of the examination of the first two formal requests, i.e. expert appraisals prior to the creation of occupational disease tables, respectively for **asbestos and ovarian and laryngeal cancers**, and **pesticides and chronic obstructive pulmonary disease (COPD)**. Work will also continue with examination of a new formal request received by ANSES for an expert appraisal on formaldehyde and leukaemia. The implementation of public, independent collective expert appraisal based on a robust and proven methodology should therefore help strengthen the scheme for recognising occupational diseases, in accordance with the objectives set by the public authorities.

[13] Socio-economic impacts of REACH authorisations. A meta-analysis of the state of play of applications for authorisation, April 2021
[14] Impacts of REACH restriction and authorisation on substitution in the EU, July 2020
[15] Substances of very High Concern: subject to authorisation under REACH
[16] Regional Committee for the Recognition of Occupational Diseases
[17] Special Commission No. 4 on Occupational Diseases of the Steering Committee on Working Conditions (COCT)
[18] High Commission on Occupational Diseases in Agriculture

Improve knowledge of hazards, exposures and risks and investigate multiple exposure situations in particular

In the past few years, the Agency has had to conduct an increasing number of complex expert appraisals in occupational health related to a specific profession or industry, or to the particular ways in which work is organised. In this approach, multiple exposure and the assessment of combined risks is a central and recurring issue. Current approaches rarely integrate workers' exposure to different hazards at a wide range of exposure levels. However, numerous studies show that this represents the reality of almost all occupational situations.

In late 2019, therefore, ANSES published the first phase of its work on health risks to workers from waste recycling activities. The working group tasked with the second phase of work to assess risks in the "household packaging" and "household waste" sectors will be set up before the end of 2021, and will continue its work in 2022.

Following the debate on the occupational health of workers in the cleaning and sanitation sector, who are subject to multiple risk factors (whether physical, organisational, biological or chemical), the Agency issued an internal request to conduct an in-depth study to identify and specify the risk factors to which these workers are exposed. Its main objectives will be to identify all the determinants – particularly of a socio-economic nature – that may affect the conditions and organisation of work, as well as their impact on worker exposure and the occurrence of health effects, but also to identify all the associated short- and long-term health effects and specify the factors that may modulate their occurrence.

As mentioned above, the Agency is involved in the growing issue of multiple exposures for the different sources of exposure, whether occupational, environmental or in everyday life. The question of the exposome also represents an opportunity for the Agency to promote and exploit the integration of its various spheres of competence. Major scientific or methodological advances on this topic, to which ANSES intends to actively contribute, are necessary and called for. The work undertaken by the Agency with its Scientific Board aims to strengthen how the exposome is taken into account in its expert appraisal activities through case studies (in particular on assessing health risks for workers associated with waste recycling activities), in order to facilitate its integration into the Agency's various activities. This consideration of multiple exposure and the exposome concept is also in line with various actions in national plans and, in particular, builds on the PST3, whose Action 1.11[19], coordinated by the Agency, led to ground-breaking original results that revealed the industry sectors and occupations most concerned by multiple exposure[20]. This action will be continued as part of the Agency's work in relation to the PST4.

Following the release into the environment of sodium valproate (the active ingredient in Depakine®) by a manufacturing plant in the south of France in 2018, the Agency was asked about the biological reference value advocated by the company for this substance, and asked to recommend an OEL and a BLV. However, the event led employees to ask broader questions about their actual exposure and the associated means of protection and monitoring specifically in the pharmaceutical production sector. The Agency was therefore asked by the General Confederation of Labour (CGT) **to conduct a review of the situation concerning the exposure of pharmaceutical industry workers to active medicinal ingredients and to question** the information available for these active ingredients, as well as the access to this data (especially for occupational physicians), and lastly to question the current regulatory provisions applicable according to the status of the substances. Here again, and without the problem being exclusively limited to these questions, attention was drawn to the issue of taking combined effects into account in this sector, as well as the possibility of drug interactions with treatments that the workers might themselves be taking. This last question clearly illustrates the need to consider the issue of chemical exposure more broadly beyond the occupational sphere, legitimising a further investigation of the issue of multiple exposure and the exposome.

[19] Action 1.11: Improve the way in which multiple exposure is taken into account and target certain occupational sectors that are particularly exposed to cumulative risks

[20] See the publication: Fourneau et al. Plan santé au travail 2016-2020 : mieux connaître la polyexposition [2016-2020 Occupational Health Plan: a better understanding of multiple exposure] Environnement, Risques and Santé, John Libbey Eurotext, 2021, 20 (4), pp.377-382

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

The issue of air pollution, in particular the risks associated with **fibres, dust and particles**, is a topic to which ANSES is particularly committed and on which it has produced a great deal of work in recent years. Therefore, besides the regular production of methodological standards and the characterisation of particles in ambient air or workplace atmospheres, the Agency will work to improve information and raise awareness on this issue in the world of work.

This firstly means maintaining ANSES's involvement in conducting expert appraisals on these questions.

At the very start of 2021, a working group was set up in response to a request from several flight crew trade unions and an association of victims of aerotoxic syndrome[21], to conduct an independent scientific expert appraisal of issues relating to aircraft cabin air quality and its consequences on health, as well as a review of current institutional recommendations on courses of action or prevention. The work is scheduled to be completed in the last quarter of 2022.

In early 2022, a working group will be set up to assess the health risks for workers present or working on the road network. This is because transport, especially road traffic, is a major source of air pollution, especially in particulate form. This is a concern for workers on the road network on a daily basis, who may be especially exposed to this pollution. This expert appraisal, in response to a formal request from the Ministries of the Environment and Labour, will seek to answer several questions. These include whether or not to establish an additional excess risk associated with exposure to road traffic for these workers compared with the general population, identification of the associated exposure determinants and their relative importance, and the contribution of the different sources (air pollution/workers' activity) to their general exposure.

Just like the Agency's 2015 work on the risks to workers associated with air pollution in underground railway areas, this work will undoubtedly again raise the question of the difference in risk management standards applied to the general population and to workers, especially for pollution by airborne particles in outdoor air, classified by the International Agency for Research on Cancer (IARC) as carcinogenic to humans. The Agency should soon be publishing the results of its expert appraisal on the scientific and regulatory origins and scientific relevance of the two measurement standards, respectively for workers (inhalable, thoracic and alveolar fractions defined by standard NF ISO 7708) and the general population (PM10 and PM2.5 particle size fractions defined by standard NF EN 12341). In the coming years, and in connection with the actions on this topic planned in the PST4, the Agency will need to increase knowledge of occupational exposure to particles and dust, identify the populations most at risk and, by 2022-2023, set up an initiative to raise awareness and provide information on the prevention of risks associated with indoor and outdoor air pollution by fine particulate matter (including ultrafine particles) and dust, in connection with work activities and in coordination with public health initiatives.

Anticipating and assessing the risks associated with the new ways in which work is organised

In just a few decades, new information and communication technologies (NICTs) have fundamentally changed the occupational landscape for workers (speed of exchanges, remote working, etc.). Virtual reality, connected objects and artificial intelligence have led to the emergence of a new generation of tools that are progressively being deployed in companies. The digital transition is therefore 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. This is why 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 puts into perspective the various lessons learned from the Agency's work on this topic.

[21] Aerotoxic syndrome refers to a condition involving a variety of physical and neurological symptoms, which may be caused by the short- and/or long-term effects of exposure to aircraft cabin air contaminated with engine oils or other agents.

For example, following its first report published in 2016 on the issue of night work and shift work, the Agency undertook to examine atypical working hours other than night work. Evenings, weekends, non-contiguous or split working hours, for example, are growing in line with new forms of work organisation. The Agency initially worked on identifying these other forms of atypical working hours, characterising the workers concerned, identifying the main risk factors they face and determining the health effects associated with these working hours. A working group to assess the potential health risks associated with these different forms of atypical working hours will soon be set up, and will publish its conclusions by the end of 2023.

The Agency will also look at the new forms of work offered by digital platforms, which are mobilising ever increasing numbers of workers because of their flexibility and the possibility of supplementary income. These activities are currently often associated with precarious social and economic conditions. Workers can be exposed to different risk factors due to the environment in which they work, the means of transport they use to get around (mostly on two wheels: bicycle or scooter) or their regular intense physical activity, not to mention the strong pressure associated with the relentless pace of work due to algorithms or customer demands. Furthermore, workers on digital platforms are mostly self-employed and therefore do not enjoy the same rights and protections as employees. This way of working also makes it more complicated to monitor their health. In response to a formal request from the CGT trade union, ANSES will therefore begin work in 2022 to assess the health risks for workers on meal delivery platforms.

After months of forced teleworking due to the COVID-19 crisis, many companies are now considering their post-pandemic operations, suggesting that its use will become more widespread. This trend now seems irreversible. A national agreement for the successful implementation of teleworking was signed on 26 November 2020 to provide a framework for its use by companies. In response to a formal request from the French Confederation of Christian Workers (CFTC) for a review of knowledge on the influence of teleworking on workers' health, the Agency proposes, due to a busy occupational health work programme in 2022, contracting with an external research laboratory to carry out an initial commented review of the available literature, which will take a multidisciplinary approach (epidemiology, toxicology, ergonomics, social sciences, economics and ecology) to the health effects of remote working. A scientific assessment of the risks may then be considered, depending on the data available.

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

Assessing risks requires the detailed characterisation of exposure, i.e. **identifying and understanding its determinants**. Thus, an analysis of the actual work activity, closely tied to labour relations, economic imperatives, the organisation of production (subcontracting, etc.) depending on company size and the industry sector, the legal context and the representations of the hazards and risks by the various players concerned, is necessary for a relevant assessment of uses and exposure.

Consequently, in addition to "expology" (exposure assessment studies), turning to disciplines from the human and social sciences – such as ergonomics, sociology, psychology – and considering socio-eco-demographic components is desirable, if not essential, in many cases. From the point of view of the company's socio-economic environment, which also affects current and future exposure conditions, an analysis of the sectors and the market structure is also necessary and could call on different trends in economic science (e.g. industrial economics, innovation economics, labour economics). An understanding and a detailed analysis of the behaviour of stakeholders – whether consumers, workers or companies – in the face of the applicable regulations, and the ability of public or private institutions to implement and enforce these regulations, are all necessary dimensions for understanding exposure situations and therefore identifying risk situations and possible means of preventing or reducing them.

The Agency's efforts to mobilise disciplines in the human and social sciences (including economics, which is being deployed within the Agency with the establishment of a dedicated expert appraisal system) need to be supported and developed. These skills are now regularly called on to tackle the various occupational health assessments carried out at ANSES.

Contribute to the development and visibility of occupational health research in France and at the 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 provides input for the expert appraisals carried out by ANSES and for the decisions of public authorities. ANSES's goals and performance contract (COP) requires the Agency to ensure that it gives greater visibility at the national, European and international levels to research in occupational (and environmental) health.

Under the National Research Programme for Environmental and Occupational Health (PNR EST), the Agency will give prominence to actions to support and facilitate occupational health research, in order to develop the knowledge and skills needed for its risk assessment missions in the medium term. The research funded within this framework takes into account occupational exposure (and multiple exposure) to chemicals, particles, magnetic fields, noise, etc. and focuses on their health impacts (respiratory health, cancer, effects on reproduction, etc.). The PNR EST has also incorporated the concept of the exposome in its definition, in order to encourage more proposals for research projects related to multiple or combined exposure.

These objectives are also in line with those of the future PST4, to which the Agency will make a major contribution, mainly regarding actions devoted to research, such as the establishment of a national occupational health research strategy to strengthen strategic planning in this area, the promotion and development of multidisciplinary research with the contribution of the human and social sciences, and the exploitation of occupational health research and studies.

Lastly, ANSES will coordinate and play a key role in a European project, "PARC – Partnership for the Assessment of Risks from Chemicals", as part of the European Union's Horizon Europe framework programme for research and innovation (2021-2027). This research partnership is designed to strengthen, harmonise and develop European capabilities in chemical risk assessment in order to protect human health and the environment, including the work environment. It is slated to start in 2022 and run for seven years, and will notably improve knowledge of exposure levels in the workplace by setting up biomonitoring studies, combining the various sources of exposure – whether occupational, environmental or from everyday life – and proposing risk assessments for chemical mixtures.

Strengthen European and international partnerships

Europe in 2021 saw the adoption of a new strategic framework for health and safety at work for the period 2021-2027, the launch of Europe's Beating Cancer Plan and the start of Horizon Europe, which should enable the implementation of PARC, thus providing a European context conducive to joint work in occupational health.

ANSES has continued to strengthen scientific exchanges with partners having similar functions, with whom it has established regular and close relationships. Some of these have been formalised by partnership agreements, whether in Europe with BAuA in Germany, and RIVM, GR and TNO in the Netherlands[22], in the United States with NIOSH, or in Quebec, Canada with INSPQ and IRSST[23]. These organisations are often consulted for contributions to expert appraisals, particularly on work already undertaken or ongoing in the various countries. Relations with EU agencies (ECHA and EU-OSHA[24]) and international bodies such as the World Health Organisation (WHO), particularly its Chemical Risk Assessment Network, or the International Agency for Research on Cancer (IARC), should be continued.

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

III. Summaries of the work programmes of the Scientific Divisions

Research & Reference Division

Regulated Products Division

Science for Expertise Division

Research & Reference Division

Introduction

ANSES's Research and Reference Division brings together nine of the Agency's laboratories, along with the Strategy and Programmes Department, 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 (65 national mandates, 13 European mandates and 29 international mandates were held by these laboratories in September 2021) and **research** activities, and **contribute to surveillance** in the areas of animal health and welfare, plant health and food safety. They also contribute to the **expert appraisals** carried out by the Agency in these areas.

The **laboratory work programme** is drafted and proposed in the form of detailed worksheets covering all the reference, research, monitoring and expert appraisal activities of the Agency's laboratories. These are then discussed with the supervisory ministries. They provide an overview of the path adopted by the various units, and can be used by managers for guidance, planning and dialogue with the supervisory ministries. These sheets, which are now prepared once every two years, were therefore presented to the supervisory ministries in autumn 2020 for the period 2021-2022. Their mid-term update for 2022 was presented to the supervisory ministries in autumn 2021.

The purpose of this note is to highlight the **main orientations and highlights for 2022 contained in these updated sheets, organised according to the six cross-cutting strategic themes** defined by the Agency (animal health and welfare; plant health; food safety; antimicrobial resistance; epidemiology and surveillance; and finally exposure and toxicity of chemical contaminants). These six themes, each promoted by a scientific director, help ensure coordination between the various entities, the efficient internal running of the Agency and the search for synergies between the laboratories' scientific units and with the risk assessment units, within their spheres of competence.

This note also presents the 2022 work programme of the Strategy and Programmes Department.

Strategy & Programmes Department

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

Efficiency

The process led by the DSP to **harmonise and consolidate the reference activities of the Agency's laboratories, with a view to improving their efficiency**, will continue in 2022, including the finalisation of the activities of an in-house working group tasked with proposing guidelines and tools for the convergence of **diagnostic reagent verification practices**. In 2022, an in-house working group will also be set up to work on harmonising practices for **calculating measurement uncertainty**, as well as a large-scale project to clarify the policy and implementation conditions for **managing and exploiting laboratory data**.

A **reference panel** will again be organised in the coming year to keep up the momentum of exchanging practices and experience between French laboratories responsible for reference activities at national (NRL) and European (EURL/EURC) levels, along with an **in-house seminar for inter-laboratory proficiency test (ILPT) coordinators**, to continue promoting sharing and the search for common solutions in work in this area.

In 2022, with the support of the laboratories concerned, the DSP will also continue making proposals to decision-makers on **specific changes to the regulations on micro-organisms and toxins (MOTs)** and adjustments in their implementation, in order to minimise the difficulties and constraints currently encountered in research and reference activities. With the support of the resource departments concerned, it will also endeavour to assist the deployment in all laboratories of the IT solution, acquired in late 2021, for managing **biological assets** within the laboratories.

Major sector-specific projects

The coming year will be marked by mobilisation for the **collective audit of ANSES's research and reference activity**, following on from the preparation throughout 2021 and then the transmission of the files to the assessors in October 2021. The DSP will therefore be actively assisting the laboratories when they present their case to the assessors in January 2022, and supporting its own record and orientations before the assessors. It will then use the audit results, with the support of the Scientific Board, to draw up a key action plan covering scientific and strategic management for the next five-year period.

Scientific coordination for each of the six cross-cutting strategic themes (animal health & welfare, plant health, food safety, antimicrobial resistance, epidemiology & surveillance, exposure & toxicity of chemical contaminants) promoted by the six scientific directors will continue in 2022. 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 or post-doctoral students under co-supervision, etc.). In the area of food safety in particular, various in-house workshops will be held in 2022 following on from those that had been organised to replace the face-to-face seminar that had to be cancelled in mid-2020 due to the COVID-19 context.

More generally, the DSP will continue its efforts to facilitate coordination and foster closer scientific ties between the teams (some of which are currently very small) through larger and more coherent scientific groups and projects. To achieve this, an appropriate lever remains the opportunity for the DSP to finance **collaborative projects between Agency teams as part of the calls for expressions of interest issued internally every 18 months**. Therefore, the projects selected in early 2020 as part of the second call for expressions of interest will be completed in 2022, and the projects selected under the call for expressions of interest issued in late 2021 will start in 2022.

In 2022, the DSP will again administer a new **call for projects for doctoral grants** to encourage the hosting and supervision of doctoral students and maintain the circulation of new ideas within the teams. This will be a joint effort with INRAE, CIRAD, VetAgro Sup and now the CEA, in order to encourage the establishment of mutual projects. It will also pay particular attention to the progress of thesis projects that had to be extended due to the delay in activities linked to the health situation.

Lastly, in 2022, the DSP will again **organise ANSES's Scientific and Doctoral Days** (JSDA) dedicated to the work of all the Agency's scientists, in a format that will be identical to that of 2021 (remote) if required by the health situation. As well as promoting the scientific excellence of the Agency's entities – and especially its laboratories – on topics of importance to ANSES, the objective is to foster synergies and exchanges of information between the Agency's scientists on its research, reference, surveillance, risk assessment and regulated products activities, while marking an important step in the training of the doctoral students hosted at the Agency.

Changes to address the challenges

In 2022, the DSP will continue to implement the **promotion and partner relations policy** adopted and published in 2020 to share or make available to public and private teams working on public health the research results, biological resources and data generated by the Agency's laboratories. The objective is to further the necessary development of health tools, while complying with ANSES's obligations of independence from private interests.

Lastly, work will continue in 2022 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 faster, more efficiently and with increased robustness, in order to safeguard public health.

Scientific and institutional cooperation

The DSP will continue to support the laboratories in **developing scientific and institutional partnerships** in an ever-changing context. It will oversee effective implementation of the framework partnership agreements signed with various research and technical organisations (INRA, CIRAD, Ifremer, ACTA, SYSAAF, etc.) and propose new structural partnerships if needed. In particular, it will continue to develop the partnership with human public health players (ANRS-MIE in particular), including by capitalising on the relationships forged or strengthened since 2020 as part of the response to be provided to the COVID-19 pandemic crisis, according to the One Health approach.

The DSP, and in particular the six scientific directors, will support the laboratories as needed to move forward with **regional partnerships**, relying on our positioning in the various COMUE university groupings and our laboratories' standing with the Regional Councils.

With regard to the **alliances** created at the initiative of the Ministry of Research, the DSP will maintain its participation in certain governance bodies of the National Alliance for Environmental Research (AllEnvi), and will aim to consolidate its position in the bodies of the National Alliance for Life Sciences and Health (Aviesan).

The process of **strengthening cooperation between NRLs and National Reference Centres (NRCs)** will be pursued in conjunction with *Santé publique France*, with the aim of further strengthening mutual knowledge and understanding, which is the basis for further cooperation, particularly in terms of contributing to the epidemiological surveillance of zoonoses.

Europe and international

The DSP, working closely with the European and International Affairs Department (DAEI), will again be devoting significant efforts in 2022 to the forging of **European partnerships for Horizon Europe**[25]. These will markedly shape the European research landscape in our fields of activity. Besides the European Partnership for the Assessment of Risks from Chemicals (PARC), which ANSES is lined up to coordinate, the DSP – supported by the DAEI – will pursue its central involvement in preparing the partnership on animal health and welfare, and will continue to closely monitor the establishment of other partnerships of interest (especially those relating to food systems and antimicrobial resistance).

The five-year (2018-2022) **One Health European Joint Programme (EJP)** will continue in 2022. This partnership project, half of which is being funded by the European Commission, brings together 44 European human and animal health institutes from 22 countries. It is being coordinated by ANSES and focuses on research in the areas of foodborne zoonoses, emerging risks and antimicrobial resistance. The DSP will continue to be closely involved in representing the Agency in the consortium within the Scientific Steering Board and coordinating our laboratories' mobilisation for the scientific activities undertaken within the EJP, in collaboration with the DAEI, which is coordinating the project.
The DSP will also approach its counterparts in other European countries to promote the organisation of a **European network of research and reference players in drinking water**.

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 the dedicated scientific and technical resources of the Ploufragan-Plouzané-Niort Laboratory.
The scientific directors will be able to monitor in their respective areas how the work implemented by the ANSES laboratories contributes to meeting the challenges of the European Farm to Fork Strategy – one of the key initiatives of the European Green Deal – presented by the European Commission in May 2020 and designed to make food in Europe healthier and more sustainable.

[25] European Union Framework Programme for Research and Innovation for the period 2021-2027

1. Animal health and welfare theme

Animal health and welfare is an area of excellence for the Agency's laboratories and represents the essential potential of French reference and research in this field. Reference and research in animal health and welfare combine high-level scientific skills and technical equipment, animal models, field experience and expertise interfacing with the Agency's other entities responsible for risk assessment and veterinary medicinal products.

This combination of skills and resources allows the Agency to be particularly responsive in supporting its supervisory ministries in the control of animal and zoonotic diseases and, where necessary, the management of 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 farming systems and their consequences on animals, on the health of professionals involved in animal production, or any possible interactions with wildlife, as well as on the safety of foods of animal origin, and on the specific health risk posed by antimicrobial resistance in veterinary medicine. It therefore provides the State with the science-based evidence that is essential for establishing and supporting the implementation of risk management measures in all these areas. Lastly, its approach to research questions relating to "animal welfare for animal health" is an original one that is able to meet society's expectations in terms of quality, safety and ethics in animal production.

The ANSES laboratories' 2022 work programme in the field of animal health and welfare intends to meet the scientific challenges of risk assessment and support for risk managers in the following areas:

- **development of methods for detecting animal diseases** for analytical reference, and methods for dispelling doubts, **which can be used on farms**;
- **understanding the pathogenesis and epidemiology of zoonotic, regulated or emerging infectious animal diseases** or those with a major economic impact on the production sectors;
- **host-pathogen relationships** and the **study of the interspecies transmission barrier**;
- prevention of animal diseases, particularly through **vaccination approaches**;
- **improving animal welfare** for the benefit of animal health.

Some examples of the planned 2022 implementation of these major strategic themes are highlighted here.

Strengthening our national and European positioning

In 2022, the Agency will continue ramping up the EURC for the welfare of poultry and other small farmed animals, which ANSES is running with its Spanish, Italian and Danish partners. Follow-up and consultation meetings with the Member States' NRCs and the competent authorities are planned for late 2021 and 2022. The Agency will continue working with its European partners to set up a future European partnership on animal health and welfare in the framework of Horizon Europe. If selected by the Commission and the Member States, this European partnership will become the keystone of European research and reference in animal health and welfare for the next decade.

Activity in 2022 mainly characterised by the consequences of COVID-19

The Agency's research activities since 2020 have been profoundly affected by the global health crisis, and the teams at ANSES have been particularly proactive in making their coronavirus research expertise available to the scientific community and the State. The Agency's work, conducted through around 20 research programmes, was used to validate mask disinfection protocols, develop ferret and hamster models that provide a better understanding of the pathogenesis of the virus, evaluate experimental treatments, and assess the role of pets in the epidemiology of the virus. Starting in autumn 2021, ANSES is undertaking different investigation programmes, on methodological development in particular, to assess the potential susceptibility of livestock to infection by the SARS-CoV-2 virus. The teams will also be involved in the European integrative project COVRIN on development and harmonisation of detection and characterisation methods for SARS-CoV-2 in humans, animals, and food and feed specimens, as part of the One Health EJP. The teams will also participate in several research programmes funded by the ANRS-MIE and will continue to support *Santé publique France* in the epidemiological analysis of data collected during the COVID-19 epidemic. In addition, long-standing work on the surveillance of coronaviruses in wildlife, brought into relief by the health crisis, will continue with our partners in 2022.

Continuation of our research on major animal diseases

ANSES will continue its work on major animal diseases, taking into account the changes introduced by the implementation of the new European "Animal Health Law"[26].

Continuation of the activities of the major experimental programme for surveillance of **low pathogenic avian influenza viruses** to establish a new surveillance protocol for these viruses, especially within the fattened duck sector, should enable intervention studies to be set up in 2022 to identify effective measures to reduce the prevalence and cases of re-occurrence of these viruses. The major health crisis during the winter of 2020-2021 has once again shown the fragility of our farms with regard to the introduction and spread of highly pathogenic AI viruses within fattened duck populations. The first epidemiological information in summer 2021 on the contamination of wild birds in the Republic of Tuva and on Lake Ubsu-Nur in Russia, and the first cases in wild and domestic birds in Northern Europe, indicate the high risk of a new epizootic in the autumn-winter of 2021-2022.

The sudden emergence of **African swine fever (ASF)** in Belgium in autumn 2018 has considerably influenced the direction of our research and reference activities, not to mention the risk assessments in this area. Recent cases affecting pig farms in Germany show that this crisis is still far from over. Our vaccinology research has been supported by an internal cross-functional programme and work on the detailed characterisation of an attenuated viral strain of ASF that can be used as a tool to identify protective factors in an oral vaccination model (a patent has been filed for this candidate vaccine). Many research programmes on this topic will be continued in 2022.

In order to respond to the emergence of outbreaks of **tick-borne encephalitis caused by the TBE virus** in Europe and particularly in France, the Agency will launch a research programme that will attempt to elucidate the biological significance of interactions between viral proteins and mammalian proteins in the pathobiology of this flavivirus transmitted by the tick *Ixodes ricinus*. The study will aim to reveal viral vulnerabilities that can be exploited for therapeutic purposes. This programme is supported by the IBEID laboratory of excellence (LabEx) on the vector competence of ticks.

The coming year will also see the launch of the Normandy Chair of Excellence (2021-25) on research into antivirals that can be used to treat horses, and the continuation of thesis work on equine viral arteritis and respiratory mycoplasma infections. A thesis on the secretome of infectious mycoplasmas will involve two of our laboratories starting in 2022.

Bovine tuberculosis, in both cattle and in wildlife reservoirs, remains a major concern for our research teams. A research programme on wildlife vaccination coordinated by two of our laboratories will also be submitted for Horizon Europe funding.

Collaborative work on Q fever with the NRC for Rickettsiosis will continue, with the implementation of serological surveys around clustered cases and the genomic comparison of human and animal strains.

Still in the area of methodological work, the development of a method for detecting ***Campylobacter hepaticus*** should improve our ability to assess the risks associated with this emerging pathogen in the free-range poultry sector.

Our active participation in the scientific work of the One Health EJP should help us continue validation of a **pan-viral chip** for identifying emerging vector-borne diseases, and study the genetic diversity and evolution of the hepatitis E virus during chronic *in vivo* and *in vitro* infections.

In the field of bee health, 2022 will see the continuation of two ambitious projects on the **complex interactions between the different stress factors affecting honeybees** (PoshBee project, funded by the H2020 programme) and on the development of air samplers to detect pesticides in bee colonies. Two new theses, respectively on viral interaction and on *Aethina tumida*, will start in late 2021 or early 2022, the latter being the result of cooperation with ITSAP in the framework of our participation in the PRADE joint technological unit.

Lastly, in the field of surveillance and subject to availability of resources within the epidemiological surveillance platform for animal health, **national surveillance of bee mortality** (OMAA observatory and winter mortality) will be relaunched.

[26] Regulation (EU) 2016/429 of the European Parliament and of the Council of 9 March 2016 on transmissible animal diseases and amending and repealing certain acts in the area of animal health (Animal Health Law)

2. Plant health theme

The increased frequency, volume and diversity of world trade in plant products, the impacts of global climate change, changes in farming practices and crop management techniques, the consequences of growing concerns about plant protection products (PPPs) and, more generally, changes in the plant health context are contributing to the emergence of new issues associated with the plant pests involved, whether in metropolitan France or the overseas territories.

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

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

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

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

A renewed regulatory framework

The **European Plant Health Regulation (EU) 2016/2031**, which is now in effect, relies on a new classification for plant pests, with Commission Delegated Regulation (EU) 2019/1702 listing priority quarantine pests for the EU that will be subject to a specific annual surveillance plan set up by each Member State, and Commission Implementing Regulation (EU) 2019/2072 listing other regulated species. Emerging pests are subject to emergency measures at European level on a case-by-case basis. In addition, France retains the option of taking action on its territory against certain pests that are no longer listed among the quarantine and regulated pests, while the French Overseas Departments and Regions (DROM) are now considered as third countries, for which specific regulations will be put in place. All these changes have modified the scope of most of our national reference mandates and require skills to be reinforced on the pests that remain targeted by these mandates, as well as methodological developments that will be useful for their early detection and epidemiological surveillance. This will mainly be achieved through a reorientation of our study topics.

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

Lastly, **Regulation (EU) 2017/625 on official controls** has led the European Commission to set up five mandates for European Union Reference Laboratory (EURL) in plant health, whose activities started in 2019. Our three EURLs (plant-parasitic nematodes, insects and mites, fungi and oomycetes) will be included in the second work programme, established for the period 2022-2023. The main objectives for this period are to organise ILPTs and training for NRLs on the detection of regulated pests.

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 *X. fastidiosa* and will also validate the method for identifying the bacterium's insect vectors, while supporting approved laboratories through the organisation of training and the transfer of analytical methods for these insects. Our activities also include maintaining the interface for consulting and visualising surveillance data in France, and analysing this data (reports and maps), as part of the tasks of the national epidemiological surveillance platform. From a research point of view, the study of the bacterium's genetic diversity will continue, as will the study of vectors other than *Philaenus spumarius*. Regarding the bacterium responsible for HLB, publication of a real-time PCR detection method is ready to be finalised, while a thesis on disease modelling in an island context (Reunion Island) will be completed. At the same time, we will be jointly coordinating the dedicated working group within the national epidemiological surveillance platform, whose objectives include providing data on HLB outbreaks in the French overseas territories and improving surveillance systems. Lastly, coordination of networks of official laboratories and participation in inter-laboratory tests for detecting the pinewood nematode on wood and in its insect vector will not only remain very active at national level, but will also take on a European dimension as part of the EURL mandate for nematodes.

At the same time, we will be increasingly focused on three other pests that have also become a major concern in France: tomato brown rugose fruit virus (**ToBRFV**), 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 included in our reference mandates, the official method for its diagnosis on plants and seeds that has been drawn up will now be implemented. For Foc TR4, the detection method will be implemented under accreditation and we will work on its surveillance via our confirmatory analyses of the first positive cases and coordination of the network of official laboratories. Lastly, the most recent detections mean that primary importance still needs to be attached to the *Bactrocera dorsalis* species complex. There will be a strong focus on this insect pest, mainly as part of EURL activities, and at the same time we will also continue to supervise a thesis aimed at validating 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 European and international levels (EFSA, EPPO and CIPV panels and working groups, H2020 VALITEST project on improving diagnostic tools for plant pests, other EURLs).

Standards, technologies and methodologies that guarantee innovation and quality

With the requirements of the new European regulations on accreditation and the need in the short and medium term for more powerful validated methods, within the meaning of the ISO/IEC 17025:2017 standard, our work for the reference mission will change in that from now on, all analyses carried out under accreditation will be according to the 2017 version of this standard. In addition, the nine types of ILPT we organise will be implemented according to ISO/IEC 17043.

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 and high-throughput sequencing techniques (Illumina, MinION), including on new matrices such as insect vectors of *Xylella fastidiosa* or HLB. Technological innovation using high-throughput sequencing will also help improve post-entry plant quarantine, detect herbicide resistance in invasive plants, and characterise the pathobiome on foodstuffs of plant origin, via a cross-cutting collaborative project under the aegis of the DSP involving several laboratories and including a health and pest risk analysis component. For GMOs, characterisation of techniques for detecting and identifying polymorphisms at the nucleotide level will continue, to enable identification of products from new breeding techniques (NBTs). Overall, bioinformatics will play an increasing part in the laboratory's activities. It is important to underline that morpho-biometric methods for identifying nematodes and insects and biological tests of PPP resistance will still require considerable effort in a context of increasing scarcity of skills that remain crucial in view of the corresponding issues.

Lastly, as part of the Horizon Scanning for Plant Health project with EFSA, an innovative methodology for monitoring the media and scientific literature will be deployed with a view to early identification of new emerging or re-emerging pests within the EU.

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

Not only will 2022 see the continuation or launch of national and international collaborative projects (EFSA on *Phyllosticta citricarpa*, ANR on phytoviruses, LabEx ARBRE on aerial dissemination of forest pathogenic fungi, CASDAR on cyst and root-knot nematodes, Ecophyto on vineyard weeds), but new structural and visible links with our academic partners will become operational. 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 **NemAlliance cluster** (INRAE Brittany-Normandy Centre) for the study of plant-parasitic nematodes, the **Mycology contracted unit** (INRAE 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), which will also begin its activities on emerging pathogen and pest populations for the French overseas territories and the South-West Indian Ocean/Southern Africa/East Africa region.

ANSES will play an ever more central role in coordinating the **national epidemiological surveillance platform for animal health** with the DGAL, INRAE, Fredon, Acta, the Chambers of Agriculture and soon CIRAD, and will co-lead or take part in working groups, mainly on surveillance schemes for regulated or emerging pests and on methodological work (international health monitoring, health reports, data quality, etc.).
In addition, our contribution to surveillance will now also include making our data available to the platform as needed, close involvement in cross-cutting support (epidemiology, biostatistics, IT) 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 biological surveillance of France being carried out by the DGAL. The list of themes to be studied will be defined during the fourth quarter of 2021.

3. Food safety theme

The food safety theme is a major and historical area for the Agency, and interacts strongly with three other cross-functional themes (antimicrobial resistance, exposure-toxicology, epidemiology-surveillance). The laboratory activities carried out under this theme cover all the main food production sectors, from farm to fork, and contribute to actions under national and European reference mandates and to surveillance of chemical and biological contaminants potentially found in food and affecting consumer and overall public health. Research in food safety is carried out to address identified problems while liaising closely with the reference and monitoring missions, generating original data for risk assessment and providing scientific input for public decision-making.

Major health challenges identified and anticipated in terms of reference and surveillance

The Agency's laboratories involved in food safety conduct reference, surveillance and research activities, and offer scientific and technical support on a vast number of chemical, biological and microbiological contaminants that may be responsible for short-, medium- or long-term adverse effects, infection or food poisoning in humans. Their work on chemical contaminants will presented through the "Exposure to and toxicology of chemical contaminants" theme below and will not generally be mentioned in this section, despite it being integral to food safety, whether these contaminants are of natural or anthropogenic origin.

The exercise of **ANSES's reference mandates is an essential mission** in food safety, placing the laboratories at the heart of the reference system supporting the competent authorities under the obligations of Regulation (EC) 2017/625. The Agency has national reference mandates for microbiological (*Salmonella*, *Listeria*, enterotoxin-producing staphylococci, *Campylobacter*, *Vibrio*, micro-organisms in water, viruses in foodstuffs of animal origin excluding shellfish, foodborne parasites) and biological (histamine, bacterial toxins) contaminants, and EU reference mandates for *Listeria* 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 Laboratory for Veterinary Services (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), which will need to be renewed in order to continue supporting and assisting the public authorities in the investigation of foodborne illness outbreaks.

Collecting or supporting the **collection of surveillance data** associated with microbiological and biological contaminants is a major challenge, because the identification and in-depth characterisation of micro-organisms allows the detection of emerging or re-emerging circulating clones, particularly virulent strains or strains belonging to a particular cluster. During 2022, therefore, the laboratories will be able to implement complementary analytical methods as part of surveillance and control plans (*Listeria*, *Salmonella*, *Campylobacter,* enterotoxin-producing *Staphylococcus aureus*, pathogenic *Vibrio* in live bivalve molluscs, parasites in fishery products, histamine and biogenic amines, marine biotoxins), the Marine Strategy Framework Directive (MSFD), the TDS3, the Biotox-Eaux network or the surveillance networks led by the Agency: *Salmonella* network, planned *Listeria* network, new laboratory network for paralytic marine biotoxins, and monitoring scheme for the emergence of marine biotoxins in shellfish.

The coming year will also see the implementation of the activities of the NRL for SARS-CoV-2 in wastewater matrices (wastewater, sewage sludge).

In addition, there are plans to systematically characterise the strains of the *Bacillus cereus* group collected in foodborne illness outbreaks, and identify the *Bacillus thuringiensis* potentially present in these outbreaks.

Lastly, **the surveillance platform for the food chain (SCA)** managed jointly by the DGAL and the DGS provides support and drives the development of food safety monitoring and the implementation of database management, in a spirit of unity among all the players involved. All the data collected, in particular on identification and characterisation of contaminants in the various food production sectors, will support **work related to risk assessment**, refine work on **source attribution**, and contribute to the **investigation of microbiological contamination from farm to fork**. The data will also be used to conduct studies and assess preventive and control measures for this contamination in the various production sectors, in particular for *Salmonella* and *Campylobacter*.

Technological and methodological innovations currently being deployed

In 2022, following a review of the organisation of WGS at the Agency with the support of the in-house next-generation sequencing (NGS) and IdentyPath platforms, the roll-out of the WGS approach **will be continued** for both second- and third-generation technologies as an extension of the cross-functional project initiated with five laboratories for the feasibility study of the MinION system. The objective for 2022 will be to deploy these NGS technologies more broadly for our reference and surveillance activities on microbiological contaminants, with a high level of responsiveness, in connection with **bioinformatics** systems tailored to the analysis and processing of data in support of the units. **Metagenomic approaches and characterisation of the mobilome and pathobiome** will also be developed in the framework of various research projects (META-DETECT thesis subject, CARAVANE transversality for *E.coli*, and pathobiome in plants, RIMICIA project).
In addition to the work associated with NGS, the high-throughput qPCR tools developed on the IdentyPath platform will be deployed for the molecular serotyping of *Salmonella* (GenoSalmo project), and the serotyping and characterisation of *Listeria* (Genolisteria project). Metabolomics studies are also being undertaken in partnership with the CNAM's agri-food chair, based in Ploufragan, as part of the METABIOT contracted unit (PAMSHA and PAMPACPO projects).

The deployment of MALDI-TOF mass spectrometry will continue through the platform, with the establishment of a spectral data library, strain characterisation in infrared spectrometry and the use of various applications to facilitate the exploitation of results. In addition, work using high-resolution mass spectrometry will be pursued for the multi-detection of marine biotoxins, the quantification of staphylococcal enterotoxins and the detection of *Bacillus cereus* emetic toxins. **Raman microspectroscopy technology** will be assessed as part of thesis work and a related project (Dormance) to determine the viability and quantify low levels of *Listeria monocytogenes* and *Listeria innocua* contamination in workshops in the fishery products sector.

A method for quantitative detection of infectious HEV viral particles by impedance measurement will be pursued and applied to different viral models including SARS-CoV-2, in order to assess infectious risk in food virology.

The **Platform for the identification of fish parasites** will provide a full range of tools and methods for detecting and quantifying parasites isolated in this sector.

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

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

The research projects carried out within the framework of the **One Health European Joint Programme (EJP)**, whether in bacteriology, virology or parasitology, are helping strengthen partnerships with the various veterinary public health, food safety and human public health institutes in Europe (H2020-EJP One Health projects Listadapt, ADONIS and DISCOVER funded under the One Health EJP). Some of these projects involve integrative, pivotal actions for the future, with the provision of reference materials and harmonisation of methodologies (H2020-One Health EJP projects TOX-Detect, CARE, HARMONY and MATRIX funded under the One Health EJP). These European partnerships may continue within the framework of Horizon Europe, especially if the future "Safe and sustainable food systems" partnership is selected. This will aim to take changes in food systems into account holistically from farm to fork by integrating environmental and food waste aspects, which could generate emerging or re-emerging hazards. In addition, partnerships with EFSA will continue to be given priority, and research work will begin on assessing the impact on/through the microbiome of the human and animal gastrointestinal tract (RIMICIA project).

Training through research as part of doctoral studies and funded projects also enables partnerships to be forged at the national level, in particular with INRAE (LILIS project on *Listeria*, *B. thuringiensis* project, TBEV project on the transmission of tick-borne encephalitis via dairy products) and the CEA (DORMANCE project), as well as at the European level (H2020 EuroBioTox, projects financed by EFSA, and future projects within the framework of Horizon Europe calls) and at the international level through a cooperative venture with the University of Montreal and the CNAM's agri-food chair (DIVERSA thesis project).

4. Antimicrobial resistance theme

Antimicrobial resistance is a major public health problem with a wide-ranging impact, involving issues of human and animal treatment, but also a threat to our ecosystems. In the animal sector, the two EcoAntibio plans deployed since 2012 (2012-2016 and 2017-2021) have achieved very significant numerical objectives for reducing animal exposure to antibiotics and the prevalence of resistant bacteria in these populations. ANSES's "Antimicrobial resistance" cross-cutting strategic theme aims to coordinate and promote synergies in the Agency's various skills on this issue, in order to provide the public authorities with the support and scientific expertise appropriate to its global 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 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 of *in vitro* or *in vivo* studies.

This work is documented in reports published and publicised on European Antibiotic Awareness Day, which is organised every 18 November.

Strengthening the effectiveness of our surveillance schemes

From 2021 onwards, implementation of **regulatory analyses within the framework of the LNR's activities** is being stepped up, in line with changes in the European directives. It remains on an alternating annual schedule – pigs and calves in odd years (2021), poultry in even years (2022) – and will continue to focus on the search for antimicrobial resistance of the bacterial species *Campylobacter*, *Escherichia coli* and *Salmonella* at the slaughterhouse when arriving (caeca) and leaving (meat). On the other hand, 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[27] network and the Vigimyc[28] network for mycoplasmas). With regard to the RESAPATH network, structural changes were finalised in 2021; these fall 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 from 2022, while the other has finalised online access (R-Shiny) to these data. In addition, a Bayesian approach will be pursued to model RESAPATH data in order to characterise changes in the susceptibility of *Escherichia coli* clinical isolates to colistin (COBAYE Project, EcoAntibio). More generally, RESAPATH will participate in the national meta-network PROMISE, financed in 2021 under the future-oriented investment programme PIA3, which will link together all the professional networks addressing antimicrobial resistance in the human, animal and environmental sectors.

In 2022, long-term monitoring of antimicrobial resistance will also be supplemented by the completion of **specific surveys** in project mode (surveillance in fish farming, in the marine environment or in veterinary hospitals, antibiotic resistance of mycoplasmas, carriage of methicillin-resistant *Staphylococcus aureus* in pigs, resistance to colistin, etc.). More generally, these antimicrobial resistance surveillance data are of great help in assessing the effectiveness of public policies on the use of veterinary antibiotics in France. They will continue to be compared with data from human medicine as identified in the interministerial roadmap (FIM) adopted in November 2016.

At European level, the Lyon Laboratory will continue directing work resulting from **the European Joint Action EU-JAMRAI (2017-2020)** (see https://eu-jamrai.eu/). ANSES, on the basis of its expertise in coordinating the RESAPATH network, was given the task of reviewing the various antimicrobial resistance surveillance systems that currently exist in veterinary medicine within Europe and the feasibility of bringing them together (EARS-Vet network[29]), and then studying the feasibility of longer-term generation of European data (Action 39 of the FIM). During 2021, various options were considered for consolidating the EARS-Vet network (COST action, inclusion in the scope of the future "AMR One Health" European partnership, a second EU-JAMRAI joint action, etc.) that could be promoted and discussed in 2022, including as part of the actions carried out by the ministries during the French Presidency of the Council of the EU in the first half of 2022 (the "PFUE 2022").

Pursuing methodological developments for the detection of antimicrobial resistance

In 2022, the Agency will pursue several actions on **methodological approaches for monitoring antimicrobial resistance**. They include developing, assessing, validating and harmonising phenotypic methods for determining susceptibility to antibiotics (IMPART and HARMONY projects within the framework of the One Health EJP; IMMUNOCOLITEST project, EcoAntibio), updating 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, and developing/standardising methods for determining susceptibility to antibiotics of different bacterial species including *Aeromonas*, *Vibrio*, *Brachyspira*, *E. cecorum*, etc. (BrachyMIC project, CoVetLab; several EcoAntibio projects) selected for their clinical or epidemiological importance or lack of existing study methods. Lastly, the Seq2Diag project, funded under PIA3 and seeking to better predict the phenotypic resistance of bacteria from their genomes, will be initiated.

[27] Surveillance network for antimicrobial resistance in pathogenic bacteria isolated from farm and companion animals in France
[28] Monitoring network of pathogenic mycoplasmas in ruminants
[29] European Antimicrobial Resistance Surveillance network in Veterinary medicine

Better characterisation of the resistome and antimicrobial resistance gene flows

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 is involved in several research projects funded by the EcoAntibio 1 and 2 plans, which will be completed (EcoAntibio 1) or continued (EcoAntibio 2) in 2022. This work will also be carried out or finalised as part of major European or international projects such as ARDIG, MEDVETKLEBS and PRE-EMPT, under the One Health European Joint Programme, etc. Lastly, the DYASPEO project, funded under the PIA3, will characterise these genetic flows between pets and humans. 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 PIA3, and of which ANSES is a member, 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. Cross-linkages with the use of biocides may 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 be studied in 2022 (e.g. SILVERPROTECT, PERSISTANCE, aDAPt projects). In connection with the ANMV's activities, the laboratories will help refine quantification of animal exposure to antibiotics through surveys on use (ongoing and/or as part of the EcoAntibio 2 plan). 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 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, vaccines) will be finalised in 2022 (RESPEC, CANIPHAGE, EVASION, EcoAntibio projects).

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

The laboratories are developing work on the topic of antimicrobial resistance in conjunction with other specialist ANSES divisions, or disciplinary fields other than those usually covered. Following the same approach as for the work on the formal request on the risks associated with antimicrobial resistance in environmental media initiated in 2018 by the Risk Assessment Department, whose conclusions were issued in 2020 and which included a contribution from the ANSES laboratories, a formal request initiated in 2021 on the **analysis of priority antimicrobial resistance risk profiles** (bacteria/resistance phenotype pairs) from the animal sector and of importance for public health will be finalised in 2022. More generally, all the interface work carried out over the last few years between laboratories and assessment departments will provide input for the debates on the construction of the EcoAntibio 3 plan in 2022, within the framework of a renewed interministerial roadmap. Lastly, 2022 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 2022, 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 analytical capacity of laboratories. As such, a project awarded under the EcoAntibio plan (REFFAO, EcoAntibio 2) will be launched in 2022 to conduct an inter-laboratory test on antimicrobial resistance in African countries, similar to what is done nationally in the RESAPATH network. Other measures, including training, will also be discussed in 2022 as part of this mandate.

5. Epidemiology and surveillance theme

The ANSES units working in epidemiology:

- provide scientific and technical support to the supervisory authorities, partner organisations and ANSES's risk assessment departments, in particular on Category 1 health hazards;
- coordinate several surveillance schemes (RESAPATH, Vigimyc, *Salmonella*, RNOEA[30], Resumeq[31], foot-and-mouth disease rapid-response unit);
- provide support to the Agency's NRLs, enabling them to fulfil their tasks of collecting, processing, facilitating access to, transmitting and disseminating epidemiological surveillance data (Order No 2015-1242 of 7 October 2015 on the organisation of surveillance concerning animal health, plant health and food safety);
- are involved in the three national epidemiological surveillance platforms (animal health, plant health and food-chain safety) in the coordination teams, operational teams and working groups;
- make a significant contribution to the production of articles for the *Bulletin Epidémiologique* on Animal Health & Nutrition published jointly by ANSES and the DGAL, in particular the annual health reviews on the surveillance of regulated diseases in animal health, and the surveillance and control plans for food-chain safety;
- conduct their own research activities.

In 2022, **they will again offer major scientific and technical support to the supervisory authorities and carry out key research on Category A,D,E diseases** such as highly pathogenic avian influenza, African swine fever (ASF), tuberculosis and brucellosis. In addition to this vital groundwork, ANSES's main orientations and significant epidemiological work for 2022 will focus on improving surveillance methods, better quantifying the role of wildlife in zoonoses and in transmission of health hazards to domestic species, the impact of livestock farming systems and conditions on animal health and welfare, vector-borne diseases and methodological research.

Improving surveillance methods

In a context where it is more vital than ever before to monitor health hazards, especially emerging ones, for both food-chain safety and animal and plant health, there is a constant need to look for new ways to improve monitoring and make it more efficient. The research carried out by the teams of epidemiologists at ANSES seeks to **propose new surveillance and alert methods**. For example, they rely on risk-based surveillance or syndromic surveillance (near-real time monitoring of non-specific health indicators such as mortality, movements, demographic data or requests for analyses). They more often include an economic approach to improve efficiency and a One Health approach to integrate all the compartments involved (human, animal, plant, environment). The feasibility of multi-faceted surveillance systems (specific, syndromic, outbreak, programmed) using data science and mega-data mining is an important area of research. In addition, following the implementation of the new European Animal Health Law, ANSES is involved in the discussions on adapting several animal health surveillance schemes.

Better quantification of the role of wildlife in the transmission of zoonoses or major animal diseases

The **wildlife compartment** plays a key role in the emergence, perpetuation or resurgence of many animal diseases and zoonoses. The coming year will be an opportunity to continue several descriptive and quantitative epidemiological studies to update knowledge on different infections/infestations in wildlife: *Baylisascaris procyonis* in raccoons, *Mycobacterium bovis* in badgers, *Anaplasma phagocytophilum* and *Borrelia burgdorferi sensu lato* in birds and foxes; these animal species have been less frequently studied so far in the epidemiological cycles of these last two bacteria.

Impact of livestock farming systems and conditions on animal health and welfare

Criticisms of the livestock sector, and "intensive" livestock farming in particular, are becoming more and more frequent. Alternative livestock systems are developing, aiming to reconcile production and societal expectations. In this context, several studies on the theme of **"rethinking livestock farming"** will continue. They will explore alternative poultry, pig and small ruminant farming systems and their consequences on animal health and welfare at the population level, but also in terms of biosecurity in livestock farming in the face of major health threats, using multi-criteria assessment approaches.

[30] National network for epidemiological observation in poultry farming
[31] Equine mortality surveillance network

Vector-borne diseases

Several **risk-modelling studies** related to health hazards determined by environmental factors, including the presence of vectors, will be initiated or continued. For example, the risk of the emergence of Rift Valley Fever in the Mediterranean basin will be analysed, mainly via the spatio-temporal variation in the basic reproduction rate R0. The eco-epidemiology of vectors associated with equine piroplasmosis will be studied in several countries. Models will be developed to assess the risk of tick bites in urban and suburban areas or during recreational activities in forests, in order to improve forecasting, and management and treatment measures. Although tick-borne encephalitis virus (TBEV) is mainly carried by vectors, in 2020 several cases of tick-borne encephalitis were associated with the consumption of goat milk products. A thesis on the risk of human food contamination by TBEV will provide more knowledge on the topic.

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. With this in mind, work on analysing contact networks and the structural risks they pose for the transmission of infectious agents will be further developed. The study of the impact of definitions of spatial and temporal units on the results from models used in syndromic surveillance will also be continued as part of a thesis in collaboration with *Santé publique France*. The use of phylodynamic tools will be extended in order to build models combining epidemiological and genetic data, and gain a better understanding of pathogen transmission. Lastly, new machine learning and deep learning approaches will enhance the tools used for time series analysis.

6. Exposure to and toxicology of chemical contaminants theme

With a view to reducing the impact of chemical contaminants on human health and the environment, the “Exposure and toxicology” cross-functional theme coordinates and facilitates collaboration between the Agency's three core divisions dealing with chemicals of anthropogenic or natural origin. The aim is to develop this area of excellence within the Agency in order to contribute to an integrative strategy for toxicological risk assessment by strengthening our ability to detect and characterise hazards, assess exposure, and monitor and control these hazards. Most of the activities of the Agency's laboratories are primarily focused on food safety, with some in animal health (bees, fish) and the environment (water). As part of the Horizon Europe programme, ANSES will coordinate the European Partnership for the Assessment of Risk from Chemicals (PARC), which creates a European network for cooperation between risk assessment entities and organisations in charge of research and reference activities. This partnership will draw up and monitor a strategic research and innovation agenda. It will develop synergies with other European partnerships and international programmes. This partnership is one of the elements of the European Union's strategy for sustainability in the field of chemicals. With the participation of 28 countries and more than 200 organisations (including three EU agencies: ECHA, EEA and EFSA), it will continue to set up a programme for chemical biomonitoring in humans, will develop cooperation on surveillance methods in the environment to supplement the current schemes for water, air and food and develop synergies on analytical tools and databases, and will develop new methodological approaches for assessing hazards and risks to humans and the environment. The teams of the Risk Assessment Department and the laboratories will contribute to the various projects set up within this framework. The establishment of the French "Hub" in partnership with *Santé publique France* will create a forum for dialogue between the different French institutes and stakeholders involved in the partnership. The major challenges identified relate to the acquisition of knowledge on several hazard classes for which the ANSES laboratories hold reference mandates, the acquisition of high-quality data for monitoring these hazards, the development of innovative surveillance approaches, and the preparation of research with our scientific partners to develop methods for analysing and characterising emerging hazards. Coordination of this partnership will help strengthen cooperation between the agencies responsible for risk assessment in both public health and environmental protection.

Major health issues identified, studied and pre-empted

The Agency's laboratories have several reference mandates for chemical contaminants of anthropogenic (**veterinary drugs, plant protection products**), natural (**marine biotoxins, histamine**) or combined (**trace metal elements and nanoparticles**) origin in food, hive products and water. Under their mandates, the laboratories will continue to develop their portfolio of analytical methods, contribute to standardisation, organise inter-laboratory tests and lead their respective networks. They will pursue the approach to improve the analysis process by participating in the Qualiplan programme. They will also prepare for regulatory changes in terms of control and surveillance limits.

With regard to **antibiotic residues**, work is focused on acquiring new knowledge on their fate in feathers and by-products and in milk. Several studies are being carried out on the influence of antibiotic residues from disinfectant biocides on antimicrobial resistance (see the “Antimicrobial resistance” theme). Besides their reference mandates, the laboratories develop analytical methods to characterise new hazards (**quaternary ammoniums and triamines, biogenic amines, microplastics, plastic additives**) in food products and water (**explosives residues, 1,4-dioxane, plant protection products and metabolites**). Data on contamination levels are thus being produced through exploratory measurement campaigns and will be useful for ongoing or future risk assessment processes at national and European level.

In order to provide updated data on the levels of exposure of the French population to substances alone or in mixtures, several units are working with the Risk Assessment Department to set up the third total diet study (**TDS3**).

Technological and methodological innovations currently being integrated

As part of their cross-functional work, the laboratories share their knowledge on the use of **high-resolution mass spectrometry** for developing broad-spectrum analysis protocols in terms of substances screened for (multiple classes), signal processing and screening for known (post-target analysis) or unknown substances, and through the creation of virtual sample libraries. The establishment of a "Kitchen Lab" would also enable the study of chemical transformations.

Regarding studies on metals, work will continue on the **speciation** of chromium, mercury and selenium, and the search for nanoparticles of titanium dioxide (TiO_2).

The analysis of **microplastics, associated additives** and **adsorbed pollutants** is being developed thanks to the platform set up in partnership with the **University of the Littoral-Côte d’Opale (ULCO)** and with the **support of the Hauts de France Region**.

The issue of analytical data storage, accessibility and reprocessing will be addressed in the framework of the European partnership and discussed in the "ANSES for Open Science" strategy.

Partnerships to better characterise the nature of hazards in relation to exposure

The PARC partnership will strengthen the collaborative work with our French and European partners to generate new knowledge that is invaluable for exposure-based hazard characterisation. Several projects integrate the development and validation of new **cell culture methods** (3D models of liver, intestine), **measurements of effects** (cytotoxicity, genotoxicity, neurotoxicity, neurodegenerative disease, intestinal microbiota), **kinetic studies** of *in vitro* and *in vivo* fate, **mathematical modelling** (use of QSAR software[32], *in vitro-in vivo* extrapolation, physiologically-based pharmacokinetic models). The projects concern different classes of substances ranging from regulated products to natural substances. In animal health, the effects of pollutants on the immune response of farmed fish will be investigated by addressing the impact of nano- and microplastics.

Analytical capabilities can also be mobilised to better understand the origins and fate of these contaminants in the environment, with work carried out on **plastics and associated pollutants** in maritime and coastal environments, or the study of the fate of **plant protection products and their metabolites** in different environmental systems (ponds, rivers, drinking water treatment systems).

[32] QSAR: Quantitative Structure-Activity Relationship

Regulated Products Division

The 2022 work programme of the Regulated Products Division will be structured around the following objectives:

- Continue improving **efficiency** by looking for ways to optimise in-house assessment and decision-making processes to help reduce the time spent examining applicant dossiers, in particular in the area of MAs/permits for plant protection products (PPPs); processing these applications remains the RP Division's priority;
- Maintain responsiveness for **work on formal requests**, particularly in the event of alerts issued by the bodies responsible for the requests, while striking a balance with work on applications, the division's core activity, which is funded by tax revenues;
- **Digitise procedures (acknowledgements of receipt, decisions, correspondence with applicants)** related to the processing of applications (for veterinary medicinal products, PPPs, fertilisers, growing media, biocides), and update and consolidate information systems, in a context of urbanisation within the Agency's information systems more generally, and in keeping with the European tools of sister agencies including ECHA, EMA and EFSA;
- Respond to the challenges facing society by providing scientific and technical support and expertise on risks, in line with **major government plans and national, European and international issues:**
  - Support the **National Biocontrol Strategy**;
  - Provide input for the debate on **Ecophyto 2+ by contributing to this plan's Scientific and Technical Committee** and to questions on the determinants of this plan's indicators (incl. the so-called NODU – number of dose unit, reflecting the level of use of PPP, etc.);
  - Be a stakeholder in **EcoAntibio**, with various tasks relating to monitoring sales data, uses (2022), advice to the supervisory ministries on the associated expert appraisals (list of critical antibiotics, etc.), and the Agency's work on resistance (see the dedicated themes). At the national level, the interministerial committee for health published a roadmap for controlling bacterial resistance to antibiotics. In addition, the Ministry of Agriculture and Food adopted and launched the second plan to reduce the risks of antimicrobial resistance in veterinary medicine (2017-2022). The ANMV is actively involved in these plans and is leading several actions;
  - Contribute to the **Pollinator Plan** (updating of the 2003 ministerial order);
  - 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.
- **Strengthen information sharing and maintain listening and dialogue**, in particular by perpetuating the platform for dialogue on the issuing of marketing authorisations for plant protection products;
- Maintain **activity and presence at both European and international levels** in the various bodies and on priority work (with EFSA, FAO, WHO, OIE, Codex Alimentarius, etc.).

1. Maintain an appropriate response to the major task of assessing products and active substances and authorising products within the RP Division's remit

The division's speciality and major challenge is assessing application dossiers (from firms holding or applying for MA and similar authorisations[33]) on the risks and effectiveness/benefits of various products: biocides, veterinary medicines, plant protection products, fertilisers and growing media.

[33] Parallel trade permits; authorisations by mutual recognition, etc.

This activity is mainly financed by **tax revenues**, which depend on the volume and nature of applications submitted. A major issue is therefore the appropriate level of taxes and tax rates. ANSES-ANMV has updated these, ensuring more appropriate levels that will be taken into account in the 2022 finance bill and its implementing texts. The division will continue to work with the Legal Affairs Department on tax rates for PPPs, fertilisers, growing media and their adjuvants, and on the debate about the business model for all the services of the Regulated Products Division (Regulated Products Assessment Department, Market Authorisations Department, Information Systems Unit and Joint Administration and Finance Unit).

Modernisation and digitisation through information systems is a second work theme, whose outcome will impact the effectiveness of work on application dossiers. This should result in benefits both internally (archiving/traceability, modernisation in line with the new societal challenges of teleworking and epidemic risks, time savings, reduced expenditure on consumables and stamps) and externally, in particular with a view to interoperability with the European systems of EMA, ECHA and EFSA. Digitisation must also face the challenge of data accessibility for risk assessment and management purposes. To this end, in the area of biocides, the **SIMMBAD platform** needs to be replaced by a more modern and up-to-date tool allowing easier consultation. The D-PHY project is in production with a view to eventually digitising the submission of dossiers and forms on plant protection products. Thanks to the VIGIE project, a new veterinary pharmacovigilance tool shared with ANSES-ANMV and the Veterinary Pharmacovigilance Centre of VetAgroSup Lyon now supplements the pharmacovigilance scheme's electronic reporting website. Lastly, business applications relating to veterinary medicinal products need to be developed in order to be able to exchange data with the European databases developed by EMA under the new Regulation (EU) 2019/6, which comes into force on 28 January 2022.

Meanwhile the assessment trajectory is still on track, with a volume that varies according to European activities, the renewal or authorisation of active substances (ASs) and the submission of applications for "product" MAs. In particular, the following should be noted:

- **Trajectory on biocontrol products on track**

  One of the challenges of the National Biocontrol Strategy is to facilitate the market entry of biocontrol plant protection products. While complying with the uniform assessment principles on which authorisations for plant protection products are based, as defined by Regulation (EU) No 546/2011, PPPs meeting the compositional criteria (nature of the active substance) for biocontrol products will continue to benefit from a priority procedure. The levers used to this end are the applicable tax (which is currently reduced by between 50 and 95% depending on the nature of the products), applications submitted without delay, and priority processing with the aim of minimising time to market. This priority has been translated in practice into annual outputs (in the form of decisions) that are systematically higher than inputs, short lead times and the processing of around one hundred applications per year since 2017.

- Implementation of the **biocides assessment programme** including European planning on Member State assessments of ASs; methodological developments.

- Assessment of non-indigenous **macro-organisms** considered beneficial to plants; control methods that are also regarded as biocontrol solutions. ANSES is continuing its assessment work, and **an internal request** in this area (signed in 2021) should lead to a clearer definition of the information required for the assessment and therefore for the application dossiers.
- Development of the expertise necessary for the ANMV to assess **new therapies in veterinary medicine**.

The division will also work to absorb and organise **new tasks**. Indeed, Act no. 2020-1525 of 7 December 2020 on accelerating and simplifying public action, Decree no. 2021-205 of 24 February 2021, and the Ministerial Order of 25 February 2021 amending the amended Ministerial Order of 7 April 1981, transferred to ANSES, on 1 March 2021, responsibility for authorising the water treatment products and processes mentioned in Article L. 1332-8 of the French Public Health Code in order to meet water quality requirements for swimming pools and artificial bathing pools. French Decree No. 2021-145 of 10 February 2021 also transferred competence from the Ministry of Health, as of 1 March 2021, for marketing authorisations for biocidal products used in the preservation of human corpses (embalming fluids) in France.

The DEPR is responsible for **assessing applications for authorisation of swimming pool water treatment products** in the transitional period, and also **assesses embalming products**.

For all these assessments and related work, European cooperation is essential: zonal assessments of PPPs, **methodological developments**, European assessments of active substances, etc. (see Part 5 for details).

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

Vigilance

Through its phytopharmacovigilance (PPV) studies and its interactions with *Santé publique France*, ANSES will keep a watchful eye on the various health signals associated with the uses of regulated products, detected mainly through epidemiological or biological monitoring studies (ESTEBAN).

It will continue its approach on exposure to products, regardless of the route, through flagship studies such as **PestiRiv (samples being collected from October 2021 to August 2022)**. The deployment of PestiRiv, a study of pesticide exposure among people living in agricultural areas, implemented by *Santé publique France* and ANSES, illustrates ANSES's commitment. This study, conducted among 1,500 adults and 750 children living less than 500 metres from vineyards and more than 1,000 metres from other crops; and 750 adults and 350 children living more than 1,000 metres from any crop, will make it possible to describe the exposure of residents living near agricultural crops to the pesticides used on these crops, identify any overexposure, and gain a better understanding of how this exposure occurs. Many sources of exposure will be explored (air, water, food, etc.).

In this field, and alongside the PestiRiv study, ANSES's work will also focus on improving knowledge in the following areas:

- exposure of the general population to PPPs, particularly via ambient air, and especially for residents in cultivated areas;
- exposure of agricultural workers;
- the impact of PPPs on biodiversity, bees and other pollinators;
- the presence of PPPs in soil;
- the specificity of the adverse effects of biocontrol products;
- cumulative exposure to PPPs in the environment.

The MA Monitoring Committee, whose scope was extended to biocides in 2019, will continue its work with regard to adaptation, feasibility and compliance of the risk management measures contained in the MAs. **This committee will be renewed in 2022** with a review of the implementation of its activities.

For plant protection products, the contribution of studies and surveillance data collected under the PPV scheme (reporting to the DER's Phytopharmacovigilance and French Observatory for Pesticide Residues Unit but coordinated by the Managing Director General of the Regulated Products Division) will be decisive, both for assessing active substances and plant protection products, and for **adapting MAs according to the results and data**.

For all active substances, the work carried out under the toxicovigilance scheme with the support of the Working Group on "Toxicovigilance for regulated products" will also enable data on cases of poisoning due to regulated products to be analysed and taken into account when issuing, amending or withdrawing marketing authorisations. The inventory work on biocides has provided input for the formal request on "biocides sold from locked cabinets", for example.

The third total diet study (TDS3) currently being prepared includes a significant component, as in previous TDSs, on **"pesticide" residues**. This will be an opportunity for the RP Division to support the DER (study leader) in terms of product expertise or assessment. The study will provide an updated snapshot of estimated pesticide exposure and contributing foods.

Lastly, with regard to authorisations already issued, the DAMM will continue its work to monitor implementation of Regulation (EU) No 2020/383, which updates Annex 3 of Regulation (EC) No 1107/2009 and sets out the list of prohibited co-formulants. **Any PPP containing a banned co-formulant must, under the Regulation, be withdrawn (withdrawal of the MA) or reformulated (modification of the composition so that no prohibited co-formulant remains in the PPP)** as soon as possible and before the legal deadline of 24 March 2023 set at European level.

In the field of veterinary medicine, the new regulation requires a novel approach to vigilance through the implementation of **signal management**. The ANMV will take part on this subject within the specific European working group being set up.

Inspection

In the area of surveillance and control, ANSES will continue to regularly offer its expertise on plant protection products to State control bodies. It also carries out support inspections of product formulation facilities in line with its resources (one FTE) and prerogatives, which will be further specified in the context of the Multiannual National Plan for Official Controls (PNCOPA). Article L. 250-2, paragraph 5 of the French Rural Code (the part relating to plant protection) expressly gives ANSES inspectors control powers "with regard to the production, formulation, packaging and labelling of plant protection products, adjuvants, fertilisers and growing media".

ANSES-ANMV's inspection mission, which is more developed (61 inspections in 2020 despite COVID-19), will continue with developments on reference standards, and in particular with European collaborative efforts on **good clinical practices (GCPs)**. This will include coordination of the joint Pharmaceutical Inspection Cooperation Scheme (PIC/S)/EMA working group for revising the annexes to the **good manufacturing practices (GMPs) for veterinary medicinal products and autogenous vaccines**, drafting a position paper on autogenous vaccines, updating the French GMPs, and participating in the PIC/S experience-sharing programme on GCP inspection.

3. Maintain support for formal requests

In addition to its main task examining authorisation applications, the RP 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. These include some that are in progress and have been enshrined through contracts (for more details, refer to the corresponding worksheets): scientific and technical support for the competent authorities as part of permanent missions such as PPV; responses to formal requests such as on PPPs containing succinate dehydrogenase inhibitors (SDHIs), neonicotinoids in connection with the exemption on the use of coated seeds for sugar beet in the context of aphid control, risk mitigation and compensation measures for pollinators, "biocides sold from locked cabinets" (conditions of sale to private individuals in relation to the risks), aroma- and phytotherapy through veterinary medicines, etc.

The division contributes to various projects led by other Agency entities whenever its expertise is useful and can be mobilised: formal request on bedbugs, botulism, actions in the field of animal health (disinfection in livestock), support for the vectors/vector control mission and related topics such as resistance monitoring, etc.

- **Exposure to SDHIs** and associated risks: ANSES will continue its assessment of SDHI fungicides, with the "SDHI" Working Group set up in October 2020, jointly led by the Risk Assessment Department of the Science for Expertise Division and the Regulated Products Assessment Department of the Regulated Products Division.

In early 2022, the Agency is scheduled to issue its opinion in response to the second internal request on "Assessment of the cumulative risks to consumers associated with fungicidal substances containing succinate dehydrogenase inhibitors via food". Moreover, the first phase of a study on the impact of environmental exposures on tumour risk in subjects at risk of hereditary SDH-related paraganglioma, conducted by teams from AP-HP and Inserm and funded by the phytopharmacovigilance scheme, was followed by the launch of the second phase, also financed by ANSES.

- **Neonicotinoids**: in late 2021, ANSES is publishing the second part of its response to the formal request on the 120-day waiver granted by the Ministerial Order of 5 February 2020. The aim, if feasible on the basis of the available information, is to refine the initial study published in December 2020 on crop rotations following the use of coated seeds, in order to limit the impact on pollinators.
- Conditions for **keeping biocides with a view to their sale**: in application of Article 76 of the French EGAlim Act, ANSES was asked to propose the categories of biocidal products intended for non-professionals for which access via over-the-counter sales should be restricted.
- ANSES-ANMV will continue the work it started in 2020 on the internal request on assessing the risks to human health and the environment of **external veterinary antiparasitics in the form of baths, showers and sprays** for ruminant herds. Regarding the internal request on the state of knowledge on essential oils and plants of interest for **phytotherapy and aromatherapy in food-producing animals**, for which work was completed in late 2021, the Agency will communicate its results to EMA and the European Commission.
- **Cross-cutting work by other entities (Risk Assessment Department) that is useful to the RP Division**: the work of the Risk Assessment Department (UEReau) on **relevant metabolites** in water continues according to the DGS's priorities, with a view to documenting reports received on the presence of certain metabolites in water analysed by the PPV scheme (a recent example being S-metolachlor). In a similar vein, the cross-cutting work of other units (on TRVs, health reference values, blood contamination limit values) contributes to the division's response to various formal requests and to the analysis of reports detected by the PPV scheme.

4. Strengthen information sharing and maintain listening and dialogue

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

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

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

ANSES will be holding scientific conferences (14/12/21) on bee health, a theme correlated with the issues of risk assessment concerning bees, and pollinators and insects more broadly, in relation to the use of biocides and PPPs.

With regard to veterinary medicinal products, ANSES will strengthen its national, European and international communication strategy, a point that appears in its 2022 strategy, particularly with regard to stakeholders.

Lastly, in the field of veterinary medicinal products, ANSES-ANMV will continue its efforts to communicate and **promote the proper use of veterinary drugs** and optimise the detection of pharmacovigilance signals. Promotion of veterinary pharmacovigilance remains a priority, and implies active communication with key partners such as practitioners and breeders.

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

The Agency, and in particular ANSES-ANMV, will continue to be at the forefront of European issues, especially in the context of the French Presidency of the Council of the EU in the first half of 2022 (the "PFUE 2022") and the **new regulation on veterinary medicinal products**, which will come into effect in January 2022.

It 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.

This is also of great importance when applications are processed at European level (European MAs for certain medicines) or on behalf of these European "sister" agencies in the framework of reporting (in particular for active substances of biocides and PPPs). The Agency will continue to participate in work arising from the entry into force on 27 March 2021 of Regulation (EU) 2019/1381 on the transparency and sustainability of the EU risk assessment in the food chain, which among other things amends Regulation (EC) 1107/2009 on PPPs.

Regarding the granting of marketing authorisations (MAs), ANSES will continue to be closely involved in the European assessment of plant protection and biocidal active substances, the zonal assessment of plant protection products (countries in the South Zone as defined in Regulation (EC) No 1107/2009), the assessment of biocidal products, fertilisers and growing media, as well as the assessment of veterinary medicinal products.

ANSES supports the competent authorities in preparing for regulatory and standardisation bodies or discussion groups and negotiations, at European (SCoPAFF[34]) and international (CCPR[35]) levels for plant protection products, in the BPC[36], CG[37] and meetings of the competent authorities and the SCBP[38] for biocidal products, participation in EPPO's herbicide panel[39], and in the CVMP[40] and CMDv[41] for veterinary medicines. It also supports the competent authorities in setting standards for fertilisers or the preparation and negotiation of delegated and implementing acts under the Regulation on veterinary medicinal products.

In order to better promote its scientific knowledge and publications, ANSES will remain closely involved in developments on methods for assessing the effectiveness and risks of products regulated at European level (estimation of exposure and risks for residents and bystanders, bees, etc.), mainly through the DEPR's participation in scientific work planned under the European "PARC" partnership or exchanges within the framework of the International Liaison Group on Methods for Risk Assessment of Chemicals in Food (ILMERAC network).

In the area of plant inputs and biocides, it will continue to hold a leading position in Europe among the rapporteur Member States for the assessment of active substances or the setting of maximum residue limits (MRLs). 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.

It will continue to participate actively in European methodological work, mainly on the cumulative effects of chemicals in general, and of plant protection products in particular, and in the revision of European guidance documents for assessing the efficacy and risks of these products. It will be actively involved in drafting the guide for the assessment of biocides generated *in situ*, in collaboration with ECHA.

[34] SCoPAFF: Standing Committee on Plants, Animals, Food and Feed Regulatory committee chaired by the European Commission
[35] CCPR: Codex Committee on Pesticide Residues
[36] BPC: Biocidal Products Committee, under the European Chemicals Agency (ECHA)
[37] CG: Coordination Group for Biocidal Products, for which ECHA provides the secretariat
[38] SC: Standing Committee on Biocidal Products
[39] EPPO: European and Mediterranean Plant Protection Organisation
[40] CVMP: Committee for Veterinary Medicinal Products, within the European Medicines Agency
[41] CMDv: Coordination Group for Mutual Recognition and Decentralised Procedures – Veterinary

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

A new European strategy for EMA and the network of agencies (HMA) came into force from 1 January 2021 for a period of five years (2021-2025). This strategy takes into account the strategic themes already identified relating to Big Data, regulatory sciences, therapeutic innovations and drug availability issues.

In addition, ANSES-ANMV is continuing its major investment in the implementation of the new European regulation on veterinary medicinal products by providing support to its supervisory ministries with the negotiation of delegated and implementing acts for the new regulation and the adaptation of French law. Lastly, it is providing significant expertise to EMA and the European Commission for discussions on the implementation of the new information systems needed.

In the framework of the PFUE 2022, ANSES-ANMV will organise two meetings of the HMA jointly with the French Health Products Safety Agency (ANSM), as well as a meeting of the European CMDv and CVMP groups, which will focus on implementation of the Regulation on veterinary medicinal products. It will also organise a seminar on herbal veterinary medicines, with the regulatory and scientific reference authorities and with industry, to clarify and discuss the possible risks posed by these products, including for humans.

With its European or international counterparts, in addition to specific ANSES-ANMV partnerships, partnership initiatives under the aegis of the General Directorate may include exchanges on scientific issues of relevance to the RP Division, although these are currently more limited due to the health situation.

More specifically, through its mandate as an OIE Collaborating Centre in the field of veterinary medicinal products, ANSES-ANMV will continue its deep commitment to combating antimicrobial resistance, in particular by setting up the OIE database and training national focal points. Similarly, it will do its best to continue providing assistance with development and sharing French expertise through the various cooperation agreements signed by the ANMV with its partners worldwide (bilateral international activity, in particular with China, but also with Saudi Arabia and Russia, with whom new agreements are under discussion).

Science for Expertise Division

In line with the strategic orientations by thematic area on the one hand, and the four strategic themes of the 2018-2022 goals and performance contract (COP) on the other, the work programme of the Science for Expertise Division is based on the set of worksheets drafted by its entities (drawing on cross-functional links within the Agency), in conjunction with its supervisory ministries and external partners. This summary documents the teams' commitment to health and safety. Without being exhaustive, it gives some perspective to major actions that contribute to increasing the efficiency and scientific robustness of ANSES's work, advancing major projects in the various specialist areas, preparing and supporting developments in response to health and societal challenges, enhancing institutional communication on the Agency's role, challenges and importance, and integrating its work at European and international level. The choices have been made for their illustrative nature, as the division's activities are the result of the entire work programme. In addition, for the communication and international parts, they concern the division's contribution to ANSES's overall work in these areas.

1. Improving efficiency and increasing the robustness of our work

By its very nature, improving the efficiency (COP Theme 5) and robustness (through scientific excellence, quality, independence – COP Theme 1) of our work relies on the contribution of a broad range of activities, measured by aggregate indicators. This is the case, for example, of compliance with contractual deadlines for formal requests (indicators 5.3.2 a/b/c of the COP), or the robustness of the process for analysing personal interests of the members of our expert groups. With regard to deadlines, and in view of certain indicators that appeared to be under pressure in 2021, **the potential of the new information system validated in October 2020 will be tapped to consolidate the monitoring of work and make progress on formal requests more visible to their sponsors**. The potential of this new information system to manage the knowledge generated by ANSES's expert appraisals will also be examined. With regard to the actual conduct of work, after more than 18 months of expert appraisals systematically carried out via remote meetings, developments in the health situation should make it possible to consider holding face-to-face meetings again, or at least a significant proportion of them. With regard to this "forced experiment", the expert appraisal coordination teams of the division's different entities will maximise the specific benefits of each configuration, while limiting hybrid meetings, whose successful implementation is beyond our facilities' current technical capacities and poses difficulties in terms of inclusivity. Feedback has led to the testing and deployment of a co-authoring tool to facilitate the integration of comments in the convergence and conclusion phases of expert appraisals.

Many of the programme's sheets provide for methodological work and make a direct contribution to improving the work's robustness. This is the case for the finalisation in 2022 of the guide to "health reference values" (Sheet 5.5.1), whose updating was initiated in 2019 following an internal request and which also benefited from contributions from the "Exposome" Working Group (see below). **Methodological issues will also be central to the work of the Social Sciences, Expertise & Society Unit (MiSSES) on developing social and economic science expertise in the Agency's work** (Sheet 8.1). Following the creation of an Expert Committee (CES) specialised in economic and social analyses, ANSES will begin to develop a methodological reference framework that can be applied to its various fields of competence in three areas of work: analysis of the socio-economic determinants of risk situations, economic assessment of a health, environmental or organisational impact, and assessment of management options. Lastly, to prepare for assessing risks associated with the contaminants measured in the total diet study (TDS3), the DER launched the DATA-TOX project (Sheet 1.2.11), to encourage the collection of more in-depth data on TRVs (metadata, information associated with the establishment of the TRV such as source studies, toxicological profile, etc.) and a broadening of the sources, using the European database (OpenFoodTox) developed by EFSA, or its equivalent at ECHA. This should speed up the process, and make the results more robust and consistent with the output of other health agencies.

Various planned tasks particularly embody the desire for greater efficiency and robustness, namely:

- The progress of three working groups operating under the auspices of ANSES's Scientific Board:
  - the **"ACCMER" WG** (Sheet 5.8.2), which plans to publish a roadmap in 2022 (description of the reference method for the four themes that structure expert appraisals: **planning, analysis of uncertainty, literature review and assessment of the weight of evidence**; decision tree to determine the appropriate level of analysis; indicators for in-house deployment) and test it on several expert appraisals. These elements will supplement the Agency's standards for expert appraisals (from guidelines through to quality procedures);
  - the **"Exposome" WG (Sheet 5.8.6), which plans to produce a report in 2022** including a proposal for an ANSES-specific scope and definition for the exposome. It will also make recommendations to facilitate **integration of the exposome into the Agency's activities**, and recommendations resulting from an action to provide advice and support for practical cases. The recommendations will also concern inclusion of the exposome in the Agency's research funding missions;
  - lastly, the **"Credibility of expertise" WG** (Sheet 8.2) which, in connection with the debates held during the symposium organised in early 2021, is examining three case studies in order to pinpoint the various factors that determine and challenge the credibility of the Agency's expertise, with a view to drawing up recommendations for ANSES.
- Work on **data consolidation and interoperability**: the results of an internal request in 2019 set out the roadmap for the development of the CIQUAL table (Sheet 1.7.2) on food composition, whose updating is a COP objective (Goal 2.2). Among the planned changes are levels of added/free sugar, levels of isoflavones in foods adapted to vegetarian diets and levels of amino acids. Furthermore, the major difficulties encountered in rapidly mobilising food databases in 2021 for the formal request on nitrites and nitrates used as additives illustrated the importance of persistent vigilance regarding groundwork on automatic data matching (Sheet 1.7.6), in order to achieve a level of operational responsiveness in line with the needs of formal requests. In terms of data, two other major projects are included in the 2022 programme: firstly, the joint debate with *Santé publique France* on optimising facilities and resources for INCA/ESTEBAN (Sheet 1.6.3), and secondly, **ANSES's contribution to the "Green Data for Health" (GD4H) action within the framework of the National Environment & Health Action Plan (PNSE4)** (Sheet 5.6.3), with a view to highlighting our dual role as a producer of public data on environmental health and a user of a broad range of data for our expert appraisal and vigilance missions.
- Led by the Vigilance Scheme Coordination Committee (Sheet 9.2.1), which stems from Theme 2.1 of the COP, methodological work in 2022 in the **area of vigilance will revolve around the drafting of a guidance document**, the vigilance schemes' equivalent of ANSES's "Fundamental principles and key points of collective expert appraisal" document. Vigilance work will also benefit from the contribution of the Scientific Board, which has agreed to take charge of supervising the RNV3P's activities, and the setting up of a group for toxicovigilance (Sheet 9.2.4) with a methodological focus on data quality and data mining, whose work may also be assisted by the recruitment of a data manager. Lastly, the method for determining causality used by poison control centres will undergo scientific validation (Sheet 9.2.5).
- With the dual aim of efficiency and robustness, leading up to the mid-2022 renewal of the permanent groups on food safety and nutrition and animal health, the Agency will begin **bringing together expertise on food and water contact materials** (Sheets 1.2.2 and 1.5.1). This rapprochement results from debates held in the framework of the internal request No. 2019-SA-0117 on "Issues relating to water contact materials and expert appraisal methods to be implemented combining competence and ethics" (see the internal report of 11 March 2020). Initially designed to overcome difficulties in recruiting competent and independent experts on the water contact materials side, we also believe that this rapprochement is consistent with the "one substance, one assessment" principle (part of the Green Deal), desired at European level and supported by ANSES.

- Lastly, the research funding activity is especially concerned by efforts to improve efficiency and robustness, since the respective changes to the budgets devolved to the different funding agencies are not comparable. While the recent results of the ANR show a selection rate of around 23%, the 2021 selection of projects under the National Research Programme for Environmental and Occupational Health (PNR EST) shows a rate of barely 10% (on the general call for projects). Coordination of the PNR EST (Sheet 10.3) will therefore need to contend with changes in the funding it can mobilise for its calls for research projects (budgeting of the IFER tax since 2019, funding of dedicated calls for endocrine disruptors – EDs), while national plans such as the National Endocrine Disruptor Strategy (SNPE2) or PNSE4 firmly underline the need to improve knowledge on risks. In this regard, **ANSES is closely involved in setting up the shared portal managed by the ANR** in order to facilitate research teams' preparation for their responses to calls for projects. The Agency is nonetheless concerned about the sustainability and adequacy of the funds in relation to the programme's attractiveness and the visibility of the PNR EST's offer. This is the only scheme driven by questions arising from expert appraisal needs. **The link with expert appraisals will continue to be supported**, for better consideration of the recommendations of expert appraisals in the shaping of research questions. On these issues, **ANSES will work closely with other initiatives designed to fund the creation of knowledge** important for health-related expert appraisals, such as the PARC partnership (see §5 below), and the PEPR project[42] on the exposome and public health, submitted by Inserm to the ANR.

2. Initiating or completing major projects

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

Taking over the assessment missions assigned to the High Council for Biotechnology: the Act on multiannual research planning, specified by the Order published on 13 October, extends ANSES's missions relating to biotechnology. From 1 January 2022, the Agency will assess the environmental and health risks of all uses of genetically modified organisms (GMOs) in the open environment, whether this relates to plants, animals, micro-organisms or medicines. It will also conduct socio-economic analyses of these uses. With gene therapy medicinal products for human use, and in addition to marketing authorisations, the ANSM may seek an opinion from ANSES on issuing early and compassionate authorisations for market access – to treat rare diseases for example. In order to implement these new missions, the Agency issued calls for applications in the summer of 2021 to bolster the groups of independent experts who carry out the scientific assessments. For the socio-economic analysis of GMOs, ANSES will rely on the expert committee set up in autumn 2021. The Agency will also set up a dialogue committee dedicated to biotechnology in 2022, to supplement its existing bodies. Its role will be to inform and exchange with stakeholders on ANSES's scientific methods and work, similar to what the Agency already does for nanotechnologies, radiofrequencies and plant protection products. With regard to general questions on the social and ethical implications of biotechnology, the National Consultative Ethics Committee (CCNE) and the Economic, Social and Environmental Council (CESE) will henceforth be responsible for reflection and public debate within the scope of their respective missions.

Related to the previous topic and as part of the extension of the report[43] produced under Action 1.5 of the COP, **the Agency is accelerating deployment of its system for expert appraisal in socio-economic analysis supported by the MiSSES** (Sheet 8.1). The growing number of requests to ANSES concerning the economic sciences confirms the need for the Agency to set up such a system, whose function is both to provide useful insights for assessment and to add to the knowledge necessary for public debate and decision-making. Continuation of the deployment begun in 2021 will involve strengthening the in-house team, **increasing the workload of the expert committee** set up in the autumn of 2021, which will be called upon initially for the methodological reference framework (see §1 above) as well as for the formal requests identified for the 2022 programme and including a socio-economic analysis component, and lastly, development of a networking dynamic. The formal requests to which this CES is expected to contribute include a cost-benefit analysis of vector control strategies, the impacts of bed bugs, plant protection products containing copper, and delivery workers used by digital platforms. Other formal requests – already initiated – will be presented to the new committee for information and possible contribution (mapping of copper uses, caterpillars with stinging hairs, antimicrobial resistance in livestock, cleaning workers, REACH restriction on creosote, etc.).

[42] PEPR: Priority research projects and equipment
[43] "Socio-economic analysis: assessment and prospects for ANSES" scientific and technical support report, January 2020

One of ANSES's major projects is its **contribution to national thematic plans being renewed: in environmental health with the PNSE4 "My environment, my health" addressed by several work programme sheets; in occupational health with the National Occupational Health Plan (PST4)**, which will start in 2022; in nutrition and health with the National Nutrition and Health Programme (PNNS); with a cross-cutting approach in support of the French National Cancer Institute for the new strategy to fight cancer, etc..

Furthermore, the division considers that the following major projects should be started or completed, depending on the case, as part of the 2022 work programme:

- Increasing momentum to become fully operational in the production of opinions prior to the amendment and/or creation of occupational disease tables, while determining the scope of the areas of expertise to ensure that the timetable is sustainable (Sheet 4.3.4);
- Continuing the formal request on "Methodology for assessing health risks for bioaerosols" (Sheet 5.8.4), by initiating a second phase, with the aim of working in the short term on the responses to the formal request, and in the medium term on building tools for assessing the risks associated with airborne transmission of biological agents;
- Finalising the expert appraisal on dietary reference values for vegetarian diets (Sheet 1.4.2);
- Finalising the opinion, including a consultation on the report, on the tool for assessing an integrated vector control strategy (Sheet 3.5.1);
- Launching the expert appraisal on bedbugs in the broader framework of preventing vector-related health effects (Sheet 3.3.2);
- Completing the assessment of the risks associated with the consumption of nitrites and nitrates (first half of 2022, Sheet 1.2.6).

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

Anticipating emerging threats and risks is one of the major themes of the COP (Theme 2) and, more broadly, constitutes the very essence of a health and safety agency.

The data collected by the various vigilance schemes led by ANSES, under the coordination of the Health Alerts & Vigilance Department (DAVS), already represent an important source of **identification of emerging threats**. In line with Goal 2.1 of the COP, therefore, the division will promote methodological advances in non-targeted data mining by automatically detecting signals (syndromic surveillance, monitoring of chronological trends in poisoning by certain agents, data mining) – Sheet 9.2.5, and data mining in occupational health – Sheet 9.1.3. For 2022, and in the spirit of the SNPE2, this approach will also be deployed as part of Sheet 5.8.5 to investigate the existence of environmental determinants of growing chronic diseases such as obesity and diabetes. Also worth to be noted, and following an alert last summer, the definition of an internal request **which requires the use of a full One Health approach** because it calls on skills in animal health, vector control and food safety to identify what are the means to prevent the extension of the **tick-borne encephalitis virus (TBEV) action** (Sheets 1.3.4, 2.2.2, 3.3.1)..
With regard to phytopharmacovigilance – Sheet 5.6.1 – one of the first tasks of the year will be to develop the new strategic framework for the period 2022-2024. **The deployment of two major studies supported by PPV: Pesti'loge, which is the pesticide measurement component of the second national housing campaign (CNL2), and PestiRiv,** the major study involving biomonitoring coupled with environmental measurements, will require significant resources. As a follow-up to the national exploratory campaign to measure pesticides (CNEP) in air, a specific analysis on lindane (Sheet 4.2.3) will be launched. In addition, the cross-cutting monitoring work managed respectively by the DRV – Sheet 10.1 – for scientific monitoring, and by the MiSSES – Sheet 8.1 – for societal monitoring, are other types of identification sources deployed.

To meet societal challenges, the division **coordinates work on cross-cutting issues that underlie societal transformation**: circular economy and changes in consumption patterns, climate change and biodiversity, consideration through the exposome of multiple exposure sources and substances, and changes in society's attitudes to animal welfare.

With regard to risk assessment, the question of the *move towards a resource-efficient economy* (circular economy) will therefore lead to a variety of work being started on pollutant concentration or environmental dissemination mechanisms. The AGEC Act adopted in early 2020 is likely to generate major work on regulations and implementation texts requiring scientific and technical support from ANSES, in various fields: in environmental health, on the risks associated with the use of non-conventional sources of water (Sheet 3.4.3); in occupational health; and in food safety and nutrition (products sold in bulk/loose).

With regard to *climate change and biodiversity*, it is worth mentioning two formal requests undertaken with the French Agency for Biodiversity on coral (Sheet 3.2.8), which should be completed in 2022; different worksheets in the field of vector control (Sheet 3.3.1 to 3); the ranking of health hazards affecting drinking water production and originating from climate change (Sheet 3.4.4, an internal request that could not begin in 2021 due to the team's unavailability); and a new action to update opinion 2012-SA-0176 on the co-exposure of bees to stress factors. An internal request is also expected to be launched in 2022 to assess the risks to bee and colony health posed by recycled and/or adulterated beeswax (Sheet 2.4.3).

In terms of *responding to changes in consumer expectations and behaviour*, ANSES will work in 2022 on monitoring the Nutri-score system as part of OQALI (Sheet 1.7.4), and on vegetarian meals (internal request, Sheet 1.4.2, to establish dietary guidelines for people following diets that exclude some or all foods of animal origin and, in the context of the EGAlim Act, to recommend food frequencies in school canteens as part of a pilot scheme to introduce vegetarian menus). An internal request to provide a scientific framework for practices that are growing in response to societal demand for animal welfare labelling (Sheet 2.4.1), which was debated within the thematic steering committee meeting in June 2021, will also be launched in late 2021. Another new theme for 2022, within the framework of Action 3 of the PNSE4: a formal request will seek ANSES's thoughts on implementation of a "Toxiscore" scheme to supplement the voluntary labelling of household products, following the report by the National Consumer Council, published in July 2021 (Sheet 3.2.9).

Meeting societal expectations also means **initiating expert appraisals in response to formal requests from stakeholders**: in 2022, work will be carried out on Sheet 4.2.1 on air pollution along roadsides and associated risks for workers. More broadly, 2022 will be marked by **numerous expert appraisals in occupational health initiated by stakeholders** (mainly at the initiative of the social partners), drawing ANSES's attention to topical themes with a potential impact on occupational health and risks: phase 2 of the expert appraisal on atypical working hours (Sheet 4.1.1), initiation of an expert appraisal on the risks for meal delivery workers (Sheet 4.1.2), initiation of an expert appraisal on the risks associated with occupational exposure to active ingredients in the pharmaceutical industry (Sheet 4.2.2). The number of different requests requires the Agency to make choices, and some work – such as that on teleworking (Sheet 4.1.3) – will have to be started later.

The division also adapts to challenges through a third type of change, **by modifying the ways in which it supports public authorities or by developing its assessment methodologies**. With regard to water-related risks, in 2022 this will mainly concern initiation of the cycle of expert appraisals in support of the transposition into French law of Directive (EU) 2020/2184 of 16 December 2020 on drinking water (Sheet 1.5.5). The coming year should also provide an opportunity to formulate proposals to the DGAL and the DGCCRF in order to change the way they work with the various stakeholders on guides to good hygiene practice (GGHPs).

Evidently, the research questions addressed by the Agency within the framework of the PNR EST (Sheet 10.3) – and especially the projects funded within this framework – make a systemic contribution to emerging or evolving issues. The number of projects submitted remains very high (299 in 2021), which reflects the considerable mobilisation of scientific communities with regard to emerging issues. **Support for developments and planning within the framework of the PNR EST will take form this year through firstly, the implementation of obligations in favour of "Open Science" and secondly, the formulation of research questions on the emergence of infectious diseases related to the environment, and questions resulting from recommendations made by the Working Group on the exposome.**

In addition, after an internal debate to develop an action strategy on participatory research based on the analysis of existing and potential options, and in application of the "ANSES 2025" action plan, the coming year will be an opportunity to undertake the first specific actions resulting from these proposals for the implementation of research projects involving citizens (Sheet 8.2). **At the same time, the Research Funding & Scientific Watch Department (DFRVS) will be the vehicle for including ANSES in the National Open Science Plan**, through participation in the Committee for Open Science (CoSO) and publication of this plan's components by the Monitoring Unit, while liaising closely with all the scientific units.

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 2022, this mainly involves the following:

- Continuing to support and contribute to the in-depth reflection and actions on risk information of the Department of Communication and Institutional Relations (DICORIS). After spending time in 2021 on the overhaul of the annual report and the creation of One Health highlights involving the DER's units, work will continue on the changes made to the editorial line and basic content for the website. At the same time and in line with the highlights of the PFUE, **the preparation of messages on ANSES's vision and contribution to the EU's chemicals strategy for sustainability** will be addressed by work involving the Science for Expertise Division;
- The probable resumption in physical form of the Paris International Agricultural Show in early 2022 will also engage the division's teams, particularly those involved in the theme of food safety and nutrition. Whether through its observatory, surveillance, vigilance or expert appraisal activities, the **division intends to help convey a message on the global nature of food in the construction of our health**, using both components of safety and of nutrition and physical activity;
- Continuing to promote PNR EST-funded work together with the DICORIS in appropriate forms given the health constraints, in order to maintain its visibility and attractiveness, despite a very busy programme in the first half of 2022 due to the PFUE; After a year in which two events were held (on nanomaterials/nanoplastics and the exposome), the feasibility of a day of "Scientific Conferences" on radiofrequencies is being examined;
- 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. To this end, 2022 will be an opportunity to survey various partners (HAS, scientific organisations, federations of health professionals, etc.) on the role they could play in this respect, and to identify ways of achieving this.

5. Europe and international

Actions in Europe and internationally are coordinated within ANSES by the European and International Affairs Department (DAEI) and are in line with Theme 3 of the COP orientations. Some of them are managed by the division's entities or call heavily on their resources, in accordance with the general orientations. Our European work in 2022 will be characterised by the FPEU, which takes place in the first semester of the year. It will require major mobilisation for the organisation of various events. For the Science for Expertise Division, in particular, this means hosting in Paris the European **Forum on endocrine disruptors**, a European event that has a particular resonance given the Agency's involvement in this theme.

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

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

- Since 1 October 2020, the Best-ReMaP Joint Action on implementation of validated best practices in nutrition, with the DER involved as leader in monitoring reformulations of processed products at European level, has been an opportunity to share and compare the OQALI practices implemented in France for many years now;
- Currently in preparation, 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).

Regarding research work for 2022, it is important to mention:

- Implementation of the **Partnership for the Assessment of Risks from Chemicals (PARC)**, which aims to provide chemical risk assessors and risk managers with new data, knowledge and methods. It will also develop the network of specialist players and the scientific skills required to address current, emerging and new challenges in chemical safety. This major topic, for which ANSES has been lined up as coordinator, is the subject of a call for proposals for these new cooperation tools ("partnerships") under Horizon Europe[44]; The Science for Expertise Division, and in particular the DER, will be actively involved in two complementary ways: seeking to advance different work packages as WP/task leader or contributor; and, through the coordination of the partnership, helping **to identify strategic priorities for the development of methods or knowledge, in line with the role that PARC needs to play, similar to the United States' NTP[45] from which it was inspired**;
- The submission and – if selected – launch of the last projects of Horizon 2020, the EU's 8th Framework Programme, on emerging issues or those requiring innovation, according to the priorities identified in the Green Deal call for projects under Horizon 2020.

And lastly, regarding work with the major European agencies:

- With EFSA, besides pursuing ongoing cooperation, launch of a **pivotal project to set up an advanced assessment system** by a group of experts, led and implemented by ANSES. Part of the work will be intended for EFSA and its panel[46] in the framework of European regulations on **food enzymes**, in order to accelerate the creation and then subsequent updating of the positive list. In terms of cooperation, EFSA and the Agency work together to promote scientific exchanges when their respective mandates appear to be similar in their questions and/or timetable on topics of great importance, while ensuring that the expert appraisal processes are respected. It should also be noted that **ANSES is involved in the EFSA Advisory Group on Data**, particularly in relation to the work carried out by ANSES in the framework of the 2021 programme on the ranking of food safety hazards and risks.
- With ECHA: there is of course the deployment of recurrent REACH activities for which the agenda is determined in conjunction with the ministries, and participation in committees (Sheet 5.2.3 to 5.2.11). In addition, the exchanges between the division's units and ECHA's teams enable them to participate in discussions on how to collectively develop the strategy on expert appraisal work in order to increase the REACH Regulation's effectiveness (for example, grouping of substances, types of data to be provided when registering, etc.). Regarding **deployment of the EU's chemicals strategy for sustainability**, and within the framework of working groups or consultations, the teams of the Science for Expertise Division will be attentive and mobilised in 2022 **to formulate comments and proposals that will enable some strategic priorities of ANSES to be implemented in its routine operations:** the "one substance, one assessment" approach, the inclusion of hazard classes for endocrine disruption in the CLP Regulation and in the equivalence criteria used for substances of very high concern (SVHC), or the requirements and conditions of access relating to the scientific data that must accompany the registration of chemicals for the proper identification of the hazards and risks associated with their use.

[44] Horizon Europe is the European Union's 9th framework programme for the funding of research and innovation, which took over from Horizon 2020 on 1 January 2021 for a period of seven years (2021-2027)
[45] National Toxicology Program
[46] Expert Panel on Food Contact Materials, Enzymes and Processing Aids (CEP)