anses
French agency for food, environmental and occupational health & safety

Investigate, evaluate, protect

ANSES 2021 work programme

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I. General orientations

I. General orientations

ANSES's work programme for 2021 is in line with the strategic orientations drawn up in late 2018 for each of the Agency's fields of activity, and consistent with the commitments made by the Agency under the 2018-2022 goals and performance contract (COP in French):

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

These orientations are also based on the national plans in which ANSES has a leadership role or to which it contributes (PNSE3 – transitioning to the PNSE4, SNPE2, PST3, PNNS, EcoAntibio, Ecophyto+, etc.).

Since 2018, the cross-functional scientific departments have been working to strengthen the coherence and efficiency of the Agency's work in each of these spheres of action by fostering a strong, cross-cutting dynamic for its research, reference and surveillance activities, and by enhancing synergies with the Risk Assessment and Regulated Products Departments. ANSES's organisation into four divisions has also improved the coordination and clarity of its activities, missions and responsibilities.

The 2021 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 and a source of ideas, in support of its usefulness for the public authorities and society:

- **Continue acquiring knowledge to support expert appraisals.** In particular, the aim is to better identify the health consequences of the exposome or changes in the behaviour and consumption habits of populations, take better account of specific vulnerabilities, and enhance assessment of the health impact of different chemical, physical or biological agents.

- **Contribute to the development of scientific methods and tools that improve risk detection and assessment** (particularly cumulative risks associated with chemicals), refine expert appraisals and reduce uncertainties (for example on identifying and attributing pathogen sources), and integrate new approaches, especially socio-economic ones.

- **Anticipate, identify and characterise health risks, including during crises**, by continuing to develop the surveillance system and strengthen all the vigilance schemes, and in particular by ensuring that emerging risks are properly understood.

- **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 the approaches into account, particularly on subjects being debated in society. The Agency is also stepping up its commitment to risk prevention and reduction policies, particularly regarding antimicrobial resistance, food safety, plant health, animal health and environmental risks.

- Reinforce the Agency's commitment to efficiency through **better management of deadlines for regulated products**.

In 2020, the COVID-19 crisis confirmed the need for a more globalised and effective assessment of health risks. ANSES's actions are increasingly taking place in a European and international context, whether they concern reference activities, risk assessment, work on regulated products, or participation in major European research projects – under the current "Horizon 2020" EU framework programme for research and innovation, or the forthcoming "Horizon Europe" ninth framework programme, which begins on 1 January 2021 and runs for seven years (2021-2027).

In 2021, three priority actions will be implemented at European level:

- **In the framework of Horizon Europe, preparation of European research partnerships and the participation of ANSES teams**: several of the partnerships that may be set up are of major strategic interest to ANSES. These include the one on animal health and welfare, in which ANSES has a particularly strong leadership role within the European working group currently 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. These three partnerships offer a chance to continue the work undertaken by the current "One Health" European joint programme (EJP), coordinated by ANSES. As they are not scheduled to start in the first wave of partnerships (planned for 2021/2022), but will form part of the 2023/2024 work programme, ANSES's role and positioning still has to be clarified and agreed with the interested partners. Of particular importance to ANSES, which is lined up to coordinate it, is the Partnership for the Assessment of Risks from Chemicals (PARC), included in the first wave. This partnership would mobilise a vast consortium involving over 25 countries and several agencies in Europe, with the aim of providing chemical risk assessors and managers with new data, knowledge and methods. It would also develop the network of specialist players and the scientific skills required to address current, emerging and new challenges in chemical safety. If this partnership is accepted for funding by Horizon Europe and Member States, the Agency will be in charge of its scientific and administrative coordination as soon as it kicks off in 2022.
- **Mobilisation as part of the French Presidency of the European Union in the first half of 2022 "PFUE 2022"**: from 2021, ANSES will be contributing to the actions and initiatives of the French authorities and preparing to carry out various activities during this period, such as hosting meetings or organising events.
- **Strengthen ties with the various EU agencies, as well as ANSES's visibility and communication on its work and relations with these agencies**: ANSES entities work closely with the competent EU agencies according to our areas of activity. These activities are expected to be ramped up and expanded, particularly those with the European Food Safety Authority (EFSA), as part of developments in relations between EFSA and counterpart agencies such as ANSES in the Member States, in the context of the new Regulation (EU) 2019/1381 on the transparency and sustainability of the EU risk assessment in the food chain. Also in anticipation of the "FPEU 2022", ANSES plans to strengthen its visibility and communication on its work and relations with the various EU agencies.

Against a backdrop of growing interest and concern about health issues, in 2021 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, in 2021 the Agency will continue ensuring that its scientific and societal expertise is made fully available to any work and discussions taking place in its areas of competence.

II. 2019-2021 strategic orientations

1. ***Food safety and nutrition***
2. ***Animal health and welfare – Animal nutrition***
3. ***Environmental health***
4. ***Plant health and protection***
5. ***Occupational health***

1. Food safety and nutrition

Preamble

Food safety and **nutritional issues** are a major societal challenge due to their economic and health consequences and 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 the COVID-19 health crisis, with expectations in terms of food safety, and changes in access to food as illustrated by the use of short supply chains.

Moreover, the full significance of implementation of the **EGAlim Act**[1], which followed the debates of France's national consultation on the food sector, has become clear in the current context through the importance attached to **improving the quality and safety of our food** at the highest level of the State. This includes a symbolic scope ("I am what I eat"), which has been clearly defined by sociologists and which goes beyond health and environmental aspects, but also other values, particularly ethical ones (fair remuneration of the players in the production sectors, animal welfare, etc.).

In an increasingly urban society (more than seven out of ten French people live in towns and cities) that is sometimes out of touch with knowledge of production methods, our fellow citizens are increasingly demanding transparency and ethics, whether this concerns animal welfare on the farm, during transport and slaughter, production methods (intensive, extensive, indoor, etc.), exposure attributable to agricultural practices (including for farmers), respect for the environment and sustainability of practices, food safety, nutritional quality, etc. This view supports **the notion of "healthy, safe and sustainable" food**, a concept that includes all the different dimensions of food and farming, "from farm to fork", including environmental aspects. In addition, new topics are being considered such as **food waste**, or the issue of **food contact materials** such as plastic packaging. These topics have taken on added importance in recent months in the context of the health crisis, where it has been necessary to review and adapt production methods and, in particular, the distribution of food to consumers.

Lastly, **new consumption trends are emerging** and the link between health and nutrition is being questioned from a societal perspective more than ever before. Indeed, food is turning out to be an essential social subject about which everyone is entitled to an opinion, because of the global health and environmental challenges it raises for the future.

ANSES is addressing these complex debates with robust scientific capabilities, drawing on research and reference laboratories on the one hand, and on risk assessment units, major surveys and observatories mobilising both the fundamental sciences and the human and social sciences, on the other. All of these strengths help 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 when well-known, remains a fundamental challenge for public authorities and consumers. This control of health hazards necessarily involves a risk assessment process that is carried out at different levels:

[1] Act No. 2018-938 of 30 October 2018 on the balance of trade 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)

- **Identifying and characterising hazards using state-of-the-art techniques**

Hazard documentation mainly relies on the activities carried out by the ANSES laboratories, whether as part of their reference and surveillance activities or research work. These actions are detailed in the laboratory work programme document and will soon be assessed as part of the collective audit scheduled for late 2021/early 2022.

In 2021, ANSES will be actively pursuing its **analytical reference** missions, with 17 national and three European reference mandates in food safety, including drinking water. A robust strategy for the **deployment of new analytical techniques** will be continued and expanded. For biological hazards, this will mainly involve genomic and metagenomic techniques for whole genome sequencing (WGS) and high-throughput detection/identification tools. Similarly, 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 (data on prevalence or contamination, etc.) through the **constant improvement of analytical methods,** in terms of their performance (specificity, reducing limits of detection and quantification – LOD and LOQ, speciation in chemistry, etc.) and adaptation to the identification of **all hazards, particularly new or emerging ones** (foodborne viruses, non-regulated substances in water such as metabolites of drugs or plant protection products, etc.) and 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, virulence factors of enterohaemorrhagic *E. coli, Listeria monocytogenes*, etc.) or by acquiring data on **host-pathogen relationships** through the laboratories' research activities. 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 in *in vivo*, *in vitro* and *in silico* toxicology will help shed light on dose-responses, and establish **toxicity reference values** (TRVs) and other safety factors. Extensive work will be carried out to update the methodology for developing health reference values. Lastly, ANSES will 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). 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. The issue of analytical data storage, accessibility and reprocessing will be addressed in the framework of the ANSES for Open Science strategy. An integrative approach to toxicological risk assessment has been initiated, which will strengthen our ability to detect and characterise hazards, assess exposure, and monitor and control these hazards.

- **Structuring surveillance and data collection**

The structuring of epidemiological surveillance, with the 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, etc.), will provide new information on the prevalence and development of various hazards, including emerging ones, within different production, processing and distribution sectors and should eventually enable them to be predicted. With the help of all its partners, the SCA Platform will contribute to the analysis of data (descriptive epidemiological data, especially on prevalence, or analytical data, with the identification of circulating virulence clusters or clones, reservoirs and food vectors of disease) that can then be used in risk assessments.

In 2021, this structuring will also involve strengthening effective data storage methods (format, validation) in order to make them available for assessments. The consolidation of ANSES's role as the **interface with EFSA** (European Food Safety Authority) and the data quality missions will remain essential actions (maintaining and improving the flow of data from the CONTAMINE database; implementing the QUALIPLAN project to ensure access to usable data; 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 and published in September 2020, mainly to implement certain of its recommendations, in conjunction with the various national actors concerned.

- **Documenting exposure and assessing health risks[3]**

Total Diet Studies (TDS), conducted at regular intervals (approximately every six to 10 years) with a specific approach each time to focus on new hazards or particular populations, are designed to estimate dietary exposure to numerous chemicals found in foods (numerous PPP[4] residues, FCM[5] migration products, etc.). These studies are essential for documenting hazards, but also exposure and therefore risks. ANSES will continue to consolidate its achievements here by carrying out **a third TDS**, to enable it to analyse the presence of certain substances, with a specific focus on organically-grown food. The coming year will be devoted to the field phase of food sampling. At the same time, analytical developments in the laboratories will enable it to broaden the number of targeted matrices and lower the analytical limits necessary for health risk assessments (HRAs). Lastly, ANSES is exploring the feasibility of carrying out a specific study in the French Caribbean to acquire contamination data and calculate exposure in order to carry out HRAs on chemicals in food, in particular for chlordecone.

- **Continuation of the ranking of hazards and foods presenting 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. Comparing hazards with different mechanisms of action (essentially acute actions for biological hazards versus chronic actions for chemicals) is a major methodological challenge, and was carried out using a multiple-criteria decision analysis (MCDA).

Plans for work to follow on from CIMAP3 are geared towards applying this approach to all food-hazard pairs using the ranking tool developed in line with the choices made by the Agency's supervisory ministries. They require determined action at national and European level to achieve convergence of data for use in modelling.

[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 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] NB: To carry out all these actions, as well as those of Theme 2, it is essential to maintain measures to document food consumption. These are presented in the elements of Theme 3: Individual and National Consumption Studies (INCA).

[4] Plant protection products

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

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 has offered a variety of measures and proposals.

- **Provide information on 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.

Contributing to this is a unique source of information on food quality: **data from the Food Quality Observatory (OQALI)**, run jointly with INRAE. Since 2018, this has included monitoring of the Nutri-score nutritional labelling system. Future plans include improving visibility of the OQALI database, which is now accessible on the Internet, monitoring the possible impacts of Nutri-score deployment on food 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, which began work on 1 October 2020.

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. The analysis campaigns planned for 2021 will include new consumption trends (organic, gluten-free, vegetarian or vegan), which will be assessed with modelling tools and published with support from partners such as *Santé Publique France*. The general public will be targeted via educational materials.

- **Documenting 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 subject is given extra importance by the fact that the lockdown period in 2020 amplified certain sedentary behaviours. It will also work on burning issues relating to 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: assessing risks and contributing to the PNNS**

ANSES will draw on data collected in the Third Individual and National Study on Food Consumption (**INCA3**), a recurring activity, to estimate food consumption, nutritional intakes and dietary exposure to chemical contaminants, in order to assess the nutritional risks associated with consumption of ultra-processed foods, and risks associated with chemical contaminants. The Agency will develop harmonised statistical and IT tools and calculation practices for quantitative risk analysis.

As part of the French National Nutrition and Health Programme (PNNS), ANSES will facilitate the exploitation of its conclusions on **consumption guidelines** for all populations, especially children, pregnant and breastfeeding women, and the elderly. Work will also be undertaken on the piloting of vegetarian menus in school canteens. 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

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

Even for well-documented hazards, it is important to take account of different routes of exposure (aggregate exposure) and of exposure to mixtures (cumulative exposure). 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. In 2021, ANSES will also focus its action on **methodological and scientific developments**, which will contribute to a better characterisation of exposure to health hazards and more specific risk assessments. This will primarily include:

- Continuation of assessments of **endocrine disruptors** as part of the SNPE2[6] and the PNSE4[7];
- Work on **biomonitoring** issues (definition of relevant markers and meaning, including the issue of "omics", and setting critical blood concentration values, etc.), with a leading role in the ongoing European human biomonitoring project "HBM4EU" and the follow-up to this project as part of the future Partnership for the Assessment of Risk from Chemicals (PARC) under Horizon Europe;
- Development and improvement of **physiologically-based toxicokinetic (PBTK) models** in order to refine risk assessments;
- Methodological work on **exposure factors**;
- **"Multi-hazard" approach by production sector** (biological hazards);
- **Source attribution** of infectious foodborne diseases;
- Proportionate consideration of **uncertainties and levels of evidence** in risk assessments;
- Differential identification of risks to **specific populations:** consideration of specific sensitivities (link with toxicology: sensitivity window for reprotoxic effects/pregnant women or neurotoxic effects/children, etc.);
- Methodology for assessing **aggregate and combined human exposure to chemicals** with a view to assessing risks;
- Development of **harmonised statistical and IT calculation tools** for quantitative risk analysis.

- **Understanding new risk factors and adjusting the risk assessments**

The INCA studies provide consumption data essential for the assessments 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 is considering the approach to be taken for jointly conducting a **new INCA4 study that responds to the recommendations** made during previous expert assessments, particularly on the specific consumption characteristics of certain population groups. ANSES needs to identify new practices or growing trends where risk assessments need adjusting in order to better factor them in and verify their possible health impacts, and maintain effective vigilance mechanisms.
For example, the INCA3 study identified practices constituting new risk factors, such as a marked increase in the consumption of raw animal foods and a tendency to consume food after the recommended use-by dates. Similarly, there has been a noticeable trend towards new products or ranges (from organic farming) or towards specific diets (vegetarian, vegan, "free from...", etc.). ANSES will continue to focus on new products, technologies, recipes and consumption patterns. Particular attention will be paid to **novel foods** within the meaning of the legislation, GMOs, by adopting an approach that focuses particularly on risk assessment methodologies rather than on individual applicant dossiers, "nanos" used in foods, newly-formed substances, and herbal food supplements, whose consumption is increasing sharply.

[6] National Endocrine Disruptor Strategy
[7] National Environmental Health Action Plan

- **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[8]) and the competence of its working group (WG) of experts on plants. These schemes have identified several adverse effects associated with the consumption of certain food supplements and a review of knowledge will be conducted in 2021. 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 actors involved and external partners (DGS, DGAL, DGCCRF, etc.). A weekly internal alert report is prepared for the Agency from the **SALSA register**; alerts from ANSES relevant to human health are forwarded to the Ministry of Health's weekly meeting on this topic.

- **Moving towards integrative assessments: "healthy, safe and sustainable" food**

A forward-looking analysis (feasibility, priority topics) on taking the **overall impact of food practices** into account, particularly in terms of sustainability, will be launched with the involvement of 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.).
Documenting **the influence of the microbiota** at different levels (influence on antimicrobial resistance, interaction of commensal and pathogenic bacterial communities, interactions between nutritional quality and health-promoting microbiota, etc.), and its inclusion in the Agency's work on food risks, is expected to be discussed during an internal preparatory debate.

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

Cooperation with ***Santé Publique France*** (foodborne illness outbreaks, PNNS, biomonitoring, particularly in the context of polluted sites and soil, etc.) is essential and will be strengthened. It will be useful to obtain updated epidemiological information on food topics, relating for example to the issue of the share attributable to exposure in chronic diseases. This close interaction ensures effective synchronisation of the missions of the two agencies without any risk of redundancy.

ANSES's **National Reference Laboratories (NRLs)** will also seek to strengthen 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 stepped up in the investigation 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 be fostered through 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.

[8] French Poison Control and Monitoring Centres

At the European 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 with the BfR, DTU-Food and RIVM, and soon with the ISS[9]. Similarly, at the international level, partnership agreements have been signed with the US-FDA, CFIA, Health Canada, NIFDS and, in the near future, with SFA[10], to allow exchanges and planning of joint projects. Targeted cooperation actions with third countries that are strategic for France and Europe (India, China, etc.) will continue. A strategy of cooperation and French contribution in Europe and internationally is expected to be established in the field of WGS analysis, following the international symposium co-organised with the partners BfR, DTU-Food and NIFDS in spring 2019.

The ongoing collaboration with EFSA will contribute to research and risk assessment work, for example on nanomaterials as food additives or assessment of food enzymes. This collaboration will be reinforced, with the support of the EFSA National Focal Point within ANSES, through ongoing funded projects or others in the evaluation phase submitted in response to calls for applications. Two examples include a project on data collection, updating and further development of biological models for humans and animal species, in order to support transparency in food and feed safety, coordinated by Wageningen Food Safety Research; and a submitted project on the development of infrastructure for WGS data analysis, coordinated by ANSES. 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.

In addition, 2021 will see the continuation of research carried out as part of various **pivotal projects**. Following the example of the European joint programme on "One Health" coordinated by ANSES, this will involve many of its scientific teams working on projects on **foodborne zoonoses, antimicrobial resistance and emerging risks**, as well as specific integrative actions to engage the Agency in a process of networking, exchanges of research equipment and scientific developments**.**

Furthermore, ANSES will apply an active and dynamic approach to building and participating in **future Partnerships as part of preparation of the Horizon Europe programme**. Indeed, the establishment of the Horizon Europe programme is a great opportunity to strengthen partnerships and cooperation. In December 2019, the European Commission proposed a 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, a **European Partnership for the Assessment of Risks from Chemicals** (PARC) has been proposed and the Agency is lined up to coordinate it. This will lead to the drafting 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 that may be set up, 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, are of major strategic interest to ANSES. These include the one on animal health and welfare, in which ANSES has a particularly strong leadership role within the European working group currently 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.

[9] 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)
[10] 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)

2. 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 2020 and proposes a few key themes for the 2021 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 2021

The coming year will be strongly marked by the consequences of the health crisis, which heavily affected our 2020 work programme, particularly for the laboratories, either by delaying certain research programmes or by requiring redeployment towards SARS-CoV-2 research activities.

A. Activity in 2020 mainly characterised by the consequences of COVID-19

Although the COVID-19 health crisis did not interrupt our reference activities in response to health alerts or surveillance programmes (avian influenza, in particular), it did significantly hamper our research activities and also led to our teams being redeployed to gain new knowledge on SARS-CoV-2. For example, our laboratories were mobilised to monitor the contamination of pets, develop ferret and hamster models for assessing new therapeutic solutions and learning more about the pathogenesis of SARS-CoV-2 viral infection, and assess solutions for recycling masks by physical decontamination (heat and UV in particular). Meanwhile the ANMV, in conjunction with the ANSM, studied the possibility of using certain veterinary drugs for humans. Concerns about the means of transmission of the virus led to formal requests on food, on contamination of domestic and livestock animals, and on the spreading of sewage sludge, for example. The French Ministry of Higher Education, Research and Innovation will fund a research programme on SARS-CoV-2 and livestock and wildlife in 2020-2021, to enable our teams and those of INRAE to develop methods tailored to the surveillance of possible animal contamination and conduct investigations in slaughterhouses. A central focus of our work in 2021 will be the continuation of our 2020 work programme and the development of the European Union Reference Centre (EURC) for the welfare of poultry and other small farmed animals. Lastly, in 2021 our laboratory teams will be preparing the scientific documents for the collective audit in late 2021/spring 2022.

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 pursue any 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 2021 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 will also be launched on the frequency at which EILAs should be organised, in order to streamline the system and ease 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 2021 will be marked by the continuation 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 in this area. In addition, research activity for EcoAntibio 2 will be marked by the launch of a programme on the detection of antibiotic use thresholds likely to trigger an excess selection of resistant bacteria. The work of the Scientific Director for Antimicrobial Resistance will be especially dependent on implementation of this plan. Programmes will also be developed to increase our knowledge of the mechanisms supporting resistance and their transfer between bacterial species, and support for therapeutic decisions will be improved through the validation of tools for the rapid detection of antimicrobial resistance on farms. In addition, in 2021, the NRL is expected to examine the first applications for validation of rapid antibiogram methods in food safety and animal health.

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 has been used to draw up EMA's recommendations to the European Commission for drafting 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. 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 also participate in 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 EcoAntibio 3 plan to be drawn up, the Risk Assessment Department has been asked to provide the DGAL with scientific information enabling it to explore the implementation of measures designed 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. ANSES is therefore leading the consortium and performing most of the reference work on poultry welfare. Awarding this first EURC mandate to France is the first official recognition of ANSES's involvement in this area. The activities of this EURC will get fully up to speed in 2021, since the teams are now in place and the first meeting of the partners of the NRCs of all the EU Member States was already planned for autumn 2020.

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, the Risk Assessment Department (Unit for the assessment of food and animal health-related risks – UERSABA) and lastly the Expert Committee on Animal Health and Welfare (CES SABA) that it coordinates.

Since September 2018, the risk assessment part of formal requests relating to animal welfare has been integrated into the CES SABA at the same level as formal requests concerning animal health, thereby fostering a holistic approach to animal welfare and health. Consideration of this issue by society has given rise to numerous initiatives in the animal production field, which will be able to take advantage of the scientific guidelines drawn up by ANSES and will have a positive impact on the welfare of farmed animals. The expert appraisal on the guide to good practices for Equidae welfare was finalised in 2020, along with the opinion on dogs likely to be dangerous, whose conclusions were largely endorsed by French Member of Parliament Loic Dombreval's report on the welfare of pets and Equidae. Similarly, ANSES published its opinion on sampling protocols for monitoring good cattle stunning practices in slaughterhouses; this should lead to improved monitoring of this essential step in animal protection at the slaughterhouse.

F. European and international activities

At the **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. Also worthy of note will be the launch of the major European project MOOD (MOnitoring Outbreak events for Disease surveillance in a data science context) on animal health surveillance systems. It is being coordinated by CIRAD with ANSES as a partner

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 2021 with, in particular, the strengthening of relations with the Friedrich Loeffler Federal Institute for Animal Health Research (FLI) in Germany, through the signature of a scientific cooperation agreement planned in the coming months.

Moreover, besides responding to calls for European projects on specific themes, ANSES will continue its work in 2021 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.

G. Outlook regarding veterinary medicinal products

The coming year in Europe will see an acceleration in the work needed to implement Regulation (EU) 2019/6 on veterinary medicinal products in January 2022. In the meantime, several delegated and implementing acts have to be adopted and new computerised databases (including on veterinary medicinal products and veterinary pharmacovigilance) need to become operational. In particular, the ANMV will continue chairing the task force set up to prepare for the entry into force of the new regulations, and maintain its leading position in the governance of work on telematics. Similarly, at national level there is a great deal of regulatory work to be done as a consequence to adapt national law.

In the area of expert appraisals, the ANMV will continue work in response to two internal requests: one on the risks associated with the use of external antiparasitics in the form of baths, showers and sprays for ruminants, and the other to assess the risks of herbal medicines in terms of consumer safety.
Work will also continue on developing the IT tools essential to the ANMV's activity and performance; the VIGIE project, which involves setting up a new long-term scalable national pharmacovigilance database, will help optimise the operations needed for managing reports to the pharmacovigilance scheme. Similarly, the ANMV will continue to examine the digitisation of processes and data within ANSES.

Lastly, the ANMV will continue **its international activities** as much as possible, depending on the progression of the COVID-19 health crisis, particularly with Morocco, Thailand and China, as well as its expert appraisal work as an OIE Collaborating Centre, participating as a trainer in continuation of the 6th cycle of focal point training, whose main themes – besides combating antimicrobial resistance – are autogenous vaccines, veterinary drug quality and pharmacovigilance.

H. Risk assessment

Risk assessment activities in animal health will target threats to France due to certain health hazards spreading across Europe. African swine fever (ASF) and *peste des petits ruminants* are getting closer to France and require preparatory measures. Our teams have been working intensely on the emergence of ASF in wild boars in Belgium. The state of emergency that has prevailed since September 2018, with many formal requests being addressed, made way in 2020 for more fundamental issues raised by the ASF action plan established by the French authorities. Our teams have also needed to maintain a high level of readiness to assess any **risk of introduction** or spread of other urgent health hazards.

France is also combating major animal diseases on its territory. This is the case with bovine **tuberculosis**, which is the subject of an eradication action plan. The fight against bovine tuberculosis touches on many scientific fields, from diagnostic methods and their use in screening through to future-oriented vaccination issues, in a particularly complex multi-host epidemiological context involving both domestic animals and wildlife.

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 in animal health-welfare and nutrition will be adapted accordingly.

Animal botulism, a potentially zoonotic disease affecting many animal species related to the environmental reservoir, will be the subject of an updated risk assessment in 2021. The subject symbolises the Agency's cross-cutting work between its research, reference and risk assessment units in the fields of animal health and food safety, while also taking the environment into account.

Lastly, regarding cattle health, concerns raised by stakeholders about the impact of foreign bodies or the possible role of wind farms are mobilising two working groups and will be addressed by Agency opinions in 2021.

In animal nutrition, work will continue on the assessment of risks associated with practices reusing downgraded foodstuffs from the agri-food industries as animal feed. This is in line with a political will to develop the circular economy, which is demonstrated, for example, by the requirement for companies to sort their biowaste for reuse. The Act of 11 February 2016 on combating food waste explicitly imposes "*reuse for animal feed*" as one of the actions to reduce waste from "**old foodstuffs**". This reclassification of products raises a number of risk assessment questions, which will constitute a major part of the animal nutrition work programme, as will the assessment of good practice guides proposed by operators in these sectors.

This work is an example of the emerging risk assessment issues raised by the circular economy, to which the Agency will continue to pay attention.

In addition, the global movement in which animal production sectors have committed to **reducing the use of antibiotics** is taking place alongside the emergence of new alternative products and new claims that will lead to formal requests by the authorities for assessments of the **scientific relevance** of certain claims, or applications for authorisation of tests for additives.

Lastly, one of the specificities of animal nutrition, due to its positioning near the start of the food chain, is that it is included in many **cross-cutting formal requests**. This includes toxicological risk assessments related to industrial accidents, such as the one at the Lubrizol plant. The state of emergency that has been in place since October 2019 will make way in 2021 for more fundamental issues.

All these activities are in line with the constant growth in collective expert appraisals, reflected in research and the implementation of **new methods**, combined with the characterisation of uncertainties and of the weight of scientific evidence, to enable ANSES to issue ever more transparent opinions on the state of available knowledge.

3. Environmental health

Health and environment issues for 2019-2021: what are the challenges facing ANSES?

The state of knowledge on the environment's influence on human health is constantly evolving: some risk factors are well known and avoidable in relation to pollution of air, water and soil, noise, exposure to harmful chemicals, etc. However, there are many unresolved challenges, whether long-standing or emerging, caused by environmental changes that may affect human health, the environment and economic activity. These include the consequences of unsustainable consumption, demographic growth and its territorial distribution (urbanisation and ageing of the population), uncontrolled industrial and technological changes, and development of the circular economy. These factors interact and their impacts are multiplied on the environment, on plant and animal species and humans. All this is aptly summarised by the concept of "One Planet, One Health". The influence of human activities on the environment also continues to grow, along with their negative impact on the climate in particular. Climate change in turn influences the environment, leading to changes in ecosystems and biodiversity.

In this context, there are numerous uncertainties due to a lack of knowledge on the effects of many agents: chemicals found in the environment (carcinogenicity, endocrine disruption, effects on immunity, metabolism, etc.), biological and/or physical agents, and their interactions with living organisms. There is uneven availability of data on environmental contamination and exposure: they are abundant on water in the environment and on drinking water and food. However, they are far less numerous when it comes to soil, air (especially indoors), dust, consumer products, discharges and waste. The combined or cumulative health effects of various agents, simultaneously or over successive periods of life, are covered by the concept of the "exposome". They pose a major challenge to knowledge.

Situations and modes of exposure and vulnerability to the effects of agents need to be identified and characterised (prenatal and postnatal development periods: pregnant women, young children, peripubertal period) along with situations where certain population groups are overexposed (work environment, residents of areas impacted by multiple pollutant releases, etc.). Similarly, the various determinants of exposure must be identified in order to shed light on sources of social and environmental inequalities and above all to identify levers for action. 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.

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. **These actions should therefore be coordinated with the various other plans**, such as the National Public Health Plan (PNSP), the National Endocrine Disruptor Strategy (SNPE2), the Ecophyto2+ Plan, the future National Environmental Health Action Plan (PNSE4) which will in 2021 follow on from the PNSE3 2015-2019, the Occupational Health Plan (PST3 and its successor), the Cancer Plan and its new roadmap, the Biodiversity Plan, the National Climate Change Adaptation Plan, the National Nutrition & Health Plan (PNNS), the Micropollutants Plan, etc.

Safety in terms of the environment and health should 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 (scientific, technical and societal monitoring, coordination of vigilance schemes);
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;
   - use methodological guides on assessing levels of evidence and uncertainties in expert appraisal work (ANSES, 2017).
3. **Develop the risk assessment tools** (cost-benefit studies, socio-economic studies, etc.) needed to ensure that risk management recommendations are better taken into account;
4. **Develop interdisciplinary methodological tools** to enable integrated risk assessment (exposome): cumulative risks, aggregate risks, human/animal/plant interfaces, use of biomonitoring and vigilance data;
5. **Support research in environmental health**, 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 represents the first step towards the "zero pollution" ambition 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)

The adoption of the Second National Endocrine Disruptor Strategy (SNPE2), signed at ANSES on 3 September 2020, will guide the Agency's work on the ED substance assessment programme. A consultation will be held on a list of substances to be examined by the Agency with a view to submitting them at European level (European REACh and CLP Regulations, etc.) on an annual basis, within the framework of an annual meeting involving several Thematic Steering Committees (interCOT). A methodology for prioritising substances with ED potential will be developed. A method for categorising these substances to discriminate between "known", "presumed" or "suspected" EDs will be developed and applied to the assessment of substances assigned to the Agency in this context. Substances with ED potential will be identified in various media, including outdoor air. 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 will be implementing 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. It will also assess this document's applicability in contexts other than for biocidal and plant protection substances, identifying any necessary adjustments for these situations where appropriate. Health reference values (TRVs[11], OELs[12], IAQGs[13], etc.) will be produced, as well as critical concentration values in biological media (see below).

[11] Toxicity reference values (TRVs)
[12] Occupational exposure limits (OELs)
[13] Indoor air quality guidelines (IAQGs)

➢ Nanoparticles

The Agency will provide scientific and technical support to the authorities, particularly by responding to the public consultation on the definition of nanoparticles, which should be harmonised at European level in view of the current differences between various regulations. In addition to the work on nanoparticles in food planned by the PNSE3, the Agency will continue its work to better understand the industrial sectors that use nanoparticles. After establishing an initial reference value for a specific form of TiO_2, it will continue its work on health reference values for nanoparticles (TiO_2, etc.) by requesting additional data from reporters of these substances, in particular under the European REACh Regulation[14]. It will continue to manage the national mandatory reporting portal. For 2021, the PNSE4 will set new deployment milestones for work on nanomaterials.

➢ Chemical mixtures and the exposome

Building on its own work (Contalait project, aldehydes in indoor air, etc.) and European projects such as EUROMIX (and its follow-on in the form of a cooperation agreement), Acropolis and HBM4EU, in which it participates or has participated, and the international progress made in this field, the Agency's task will be to lay the methodological foundations for ranking the priority chemical mixtures to be taken into account in its expert appraisals. This will also be in line with work that the Agency will undertake to identify the methodological foundations for clarifying the concept of the exposome and its use in health-related expert appraisals.

➢ Health reference values

Toxicity reference values (TRVs), occupational exposure limits (OELs), indoor air quality guidelines (IAQGs), biomarkers of exposure (BMEs) and biological limit values (BLVs) are essential tools for quantitative risk assessment. Critical concentration values in biological media must be developed in order to assess risks and guide public action in the event that there are BMEs to contaminants to which the population is exposed through multiple routes (ingestion, respiratory, dermal). This work will focus on the needs related to situations involving industrial sites (classified installations for environmental protection – ICPE) and polluted sites and soil. Methodological work will be carried out on developing TRVs, mainly for chemical mixtures, in order to take advances in toxicology into account and better meet the challenges of health risk assessment. 2021 will be a key year for the revision of the Agency's methodological guide.

➢ European REACh and CLP Regulations

Work on chemicals in the framework of the REACh and CLP[15] Regulations will include the assessment of substances listed in the Community Rolling Action Plan (CORAP) and a re-assessment of 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 (SVHC), 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 several new proposals for the classification of chemical substances. It is important to coordinate the Agency's work with other European agencies because of the sectoral segmentation of the substance assessment methods. One example is the circular economy, a major emerging issue. This is reflected in the European Commission's adoption on 11 March 2020 of a new action plan for the circular economy, which is one of the main elements of the European Green Deal, Europe's new agenda for sustainable growth. New EU policy (October 2020) resulting from the deliberations of the European Commission's new term of office will have to be integrated (for the aspects that concern us) in our expert appraisal work.

[14] European Regulation (EC) No 1907/2006 of 18 December 2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACh) came into force on 1 June 2007

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

- **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 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 efficacy. The Agency can also fund specific studies to encourage the production of new knowledge needed for its expert appraisal work.

Monitoring the adverse effects of plant protection products (PPPs) on humans, plants and animals and more generally on all environments, and keeping track of resistance, is the core purpose of PPV. Its actions will be strengthened to take account of biodiversity, the presence of PPP degradation products in the environment and the impact of the increasing use of biocontrol products. Work will be directed towards the identification of substances of concern, mixtures and cumulative exposure. Four strategic themes will be developed: ambient air; exposure and impacts on agricultural workers; bees and pollinators; biodiversity and environments (soil).

- **Biocides**

The issues identified for the coming years in terms of assessing the health and environmental impacts of biocidal active substances and products are similar to those presented above for plant inputs. They concern 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 – particularly regarding vector control and public health – are effective. On the subject of vector control, the limited number of solutions available on the market means that assessments are being directed towards the effectiveness of alternative methods and vigilance with regard to the rise in resistance.

The scientists involved in assessing biocides will therefore contribute to a wide range of work on developing or optimising assessment methodologies, most often carried out in partnership with other organisations or as part 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 risks and efficacy. The Agency may also fund specific studies to encourage the production of new knowledge needed for its expertise. Lastly, the Agency will continue issuing marketing authorisations for biocidal products in a context of future uncertainty regarding the number of applications to be examined.

- **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 questions on the safety of numerous products. Work in this area is expected to focus on identifying new product uses resulting from recycling, as well as the environmental dispersion of plastics in different matrices or their reuse and consequences in terms of health effects. The new French legislative context resulting from the AGEC Act (against waste and for the circular economy) is likely to keep the Agency busy on this issue.

Ranking the chemicals (e.g. flavourings) that may be found in new **tobacco and vaping products** and taking inhalation effects into account should also identify mixtures that potentially work in synergy with nicotine or other factors to maintain addiction. Work will be conducted to document the uses and exposure models of these products with a view to assessing the risks, while 2021 will also see completion of the Agency's first roadmap since it took over the mission following implementation of the 2014 European directive.

- **European and international work on chemicals**

The Agency will continue to take part in European projects such as the European Human Biomonitoring Initiative – HBM4EU 2017-2021 (co-funded by Horizon 2020): ranking chemicals of interest and defining health guidance values for biomarkers of exposure (bisphenols, perfluorinated compounds, etc.). It will begin its involvement in the Second European Joint Action on Tobacco Control (JATC2). 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.

These approaches should also be seen in the context of **the Agency's active support for the creation of an inter-agency European fund for the toxicological study of agents of public health interest**, designed to improve knowledge of the hazards and effects of a large number of agents, whether chemical (toxicological, ecotoxicological studies) or physico-chemical (nanoparticles, etc.), in addition to processes. After several years of engagement, and thanks to the new tools of European research partnerships under "Horizon Europe", the prospect of its realisation in 2021 is emerging very seriously. Indeed, this Partnership for the Assessment of Risk from Chemicals (PARC) would aim to provide chemical risk assessors and risk managers with new data, knowledge and methods. It would also develop the network of specialist players and the scientific skills required to address current, emerging and new challenges in chemical safety. If the Member States' interest in this partnership is confirmed and the proposal to be submitted in 2021 is accepted for funding, ANSES would be responsible for both scientific and administrative coordination from its launch in 2022.

Main challenges relating to water

The EU's project to revise Directive 98/83/EC on the quality of water intended for human consumption has made good progress and will now move into the implementation phase to address this important public health issue. It will lead to a redefinition of the way ANSES works at the French and European levels on materials in contact with water. It also raises multiple questions about the assessment of past or emerging risks related to regulated or non-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, as well as the issue of the effects of mixtures. The development of antibiotic resistance phenomena among bacterial strains with dispersion in environmental media is also a subject of major importance justifying continued activity in this field: work on the mechanisms underlying the selection and transmission of antibiotic resistance via the environment. 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.

Main challenges relating to air

The EU's "fitness check" of the European directives on ambient air quality (Directives 2008/50/EC and 2004/107/EC) required scientific and technical monitoring and support for the supervisory ministries. Several expert reports have been published that will provide input for this work (pesticides in air, emerging non-regulated pollutants, ambient air quality standards, etc.). Among the main issues that the Agency will have to address are mixtures of substances in the air, work on particles (ultra-fine particulate matter, nanoparticles, physico-chemical composition, and scientific and regulatory standards) and settled dust in indoor and outdoor air (risk assessment, proposed guideline values, etc.).

Health effects associated with biological agents or bioaerosols (mould, toxins, plant pest species) are becoming better known (allergies, infections, etc.) and warrant greater emphasis when assessing health risks in the context of climate change. Their urgency was highlighted by the COVID-19 health crisis.

This 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 their accessibility for expert appraisals and research. The relevance of foresight studies could be discussed with a view to estimating the health risks in the medium term.

Main challenges relating to physical agents

Assessing hazards and exposure to non-ionising radiation and its determinants is a subject surrounded by scientific and societal controversy that justifies the Agency's involvement. The development of technological innovations in different frequency ranges (digital communication technologies, etc.), with their rapid spread across all economic and social activities, raises questions about their effects on health (cognitive disorders, addictive behaviour, etc.) and the environment insofar as they constitute new sources of individual and collective exposure to electromagnetic fields, modify behaviour, and can induce indirect health effects as a result of their use (e.g. sedentary behaviour, accidents). Assessing these effects and the conditions of use and exposure, particularly in the context of the deployment of 5G, is an important issue for the Agency, especially in relation to situations of overexposure or vulnerable populations (children). 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 parallel with the work on 5G, an updating of the relationship between radiofrequencies and cancer was also launched in 2020.

The extra-auditory effects of noise are becoming better known (diabetes, etc.) and justify the updating of the expert appraisal carried out by the Agency in 2013, with an update of the methodology for assessing effects, particularly those related to interactions with other exposure (chemicals). A debate should also be undertaken on changes in sources and modes of exposure to noise with a view to assessing the health impacts in light of specific territorial characteristics (typology of housing and its changes, social environment, etc.).

On the question of stereoscopic vision, work will continue on virtual and augmented reality, particularly through the use of virtual immersion headsets, both for domestic and professional use. Like the other physical agents studied, these new technologies raise the question of identifying what constitutes exposure to risk.

Main challenges relating to vectors

On 1 January 2018, the Agency was entrusted with the expert mission for risk assessment in the field of vectors and vector control (VC) for human, animal and plant health. A dedicated working group has been set up and ANSES has carried out some initial urgent expert appraisals on vector control in the context of a dengue epidemic on Reunion Island.

Assessing the effectiveness of VC strategies is an essential challenge for the Agency in a context of spatio-temporal extension of insect vectors of pathogens for humans, animals and plants, development of resistance of vectors to conventional biocidal treatments, preservation of biodiversity, benefit-risk balance of approaches integrating the various related issues, etc. This mission will entail the development of work on expert appraisals, methodological approaches and guides, coordination and monitoring, and information.

Continued support for research by the National Research Programme for Environmental and Occupational Health (PNR EST) is essential to address challenges relating to knowledge.

4. Plant health and protection

Plant health and protection issues: what are the orientations for ANSES for the period 2019-2021?

This challenge is being addressed by two ANSES laboratories: the Plant Health Laboratory (LSV) and the Lyon Laboratory, and by three of the Agency's assessment and decision-making departments: the Risk Assessment Department (DER), the Regulated Products Assessment Department (DEPR) and the Market Authorisations Department (DAMM), which are all involved in the field of plant health and protection.

A. General points on context and internal organisation

France's agricultural, forestry, ornamental and environmental plant health situation is affected more and more by 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 led to 2020 being declared the International Year of Plant Health by the United Nations General Assembly (https://www.ippc.int/en/iyph/)

In addition, changes to the regulatory context that primarily aim to promote the use of biocontrol products and reduce the number and quantity of plant protection products (PPPs) used, which stem from growing concerns about the impact on health and the environment of treating crops, forests or non-agricultural areas with PPPs, also have a major impact on 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, or lead to the emergence or re-emergence of new plant health issues. It should also be emphasised that France possesses considerable overseas territories, which are ecologically fragile and particularly exposed.

With regard to the laboratories within the Research and Reference Division, the LSV's thematic and technical units (bacteriology, virology, GMOs, entomology and invasive plants, mycology, nematology, quarantine, pests and tropical pathogens) carry out reference missions (as the National Reference Laboratory, and – for three of them – the European Union Reference Laboratory) and research missions in plant health on phytopathogenic agents, regulated or emerging pests, invasive plants and detection of GMOs, as well as providing 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, part of the work of its Unit for Epidemiology and Support for Surveillance (EAS Unit) involves providing assistance with the development of epidemiology activities and contributing to national surveillance in the area of plants.

Regarding the departments involved in expert appraisals for risk assessment, **the DER belongs to the Science for Expertise Division**. Its scope encompasses the work of the Expert Committee (CES) on "Biological risks for plant health", with scientific and technical support from the LSV, and the work of the Phytopharmacovigilance and Observatory of Pesticide Residues Unit (UPO), which manages a scheme for detecting and monitoring resistance and the adverse effects of PPPs on human health, fauna, flora and the environment (phytopharmacovigilance). **The DEPR, part of the Regulated Products Division,** assesses the hazards and risks to humans, animals and the environment, as well as the agronomic benefits, of 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". Lastly, **the DAMM, part of the Regulated Products Division,** 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 (MA) Monitoring Committee, and product control and inspection activities.

A comprehensive approach to plant health and protection, which involves studying pest interactions with the plant and its environment, therefore helps position the Agency's activities in the general health, economic and societal context. The Agency's mobilisation and active contribution will continue in Europe and internationally, whether in risk assessment, research and reference, or monitoring, surveillance and vigilance. It will be 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 elsewhere in the world (Canada, United States, the countries of the Maghreb, etc.).

B. Main outlook for 2020-2021 in plant health and protection

➢Plant health: from risk assessment to national surveillance

Six pests will now receive particular attention in the current French plant health landscape: three that follow on from the previous work programme: the bacterium *Xylella fastidiosa,* the bacterium responsible for yellow dragon disease also known as huanglongbing (HLB), and the pinewood nematode; as well as three others that have also become a major concern in France: 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

Within the LSV's Expert Assessment of Biological Risks (ERB) Unit, which reports functionally to the DER, the formal requests to be addressed cover a variety of issues related to arable crops (alternative methods to neonicotinoids for controlling aphids on beet), arboriculture (effectiveness of sanitation methods for *Prunus* contaminated by plum pox (sharka) virus, control strategy against *Xylella fastidiosa*) or natural and green spaces (analysis of the risks of stinging caterpillars to human health and biodiversity, control strategies against canker stain of plane trees). 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 (the virus responsible for sharka on apricot, peach or plum trees), ornamental trees (the fungus *Ceratocystis platani* responsible for canker stain of plane trees) and biennial crops (aphid-transmitted viruses causing beet yellows).

These assessments will encompass:

- assessment of the effectiveness of management measures;
- assessments of control strategies;
- research into alternative control methods to neonicotinoid plant protection products;
- a joint risk analysis for humans and biodiversity.

A major new orientation of our assessment mission will be the deployment of an approach to anticipate emerging risks, through continuation of an EFSA-funded European "horizon-scanning" research programme designed to conduct a prospective analysis by monitoring the media and scientific literature in order to identify new emerging plant pests. It will aim to identify relevant information on pests that could be a source of concern for the territory of the European Union.

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

The LSV's reference mission will remain its structuring activity. To continue to respond promptly to the authorities' needs regarding biological monitoring of the country, including for emerging threats, and provide identification services to the agricultural profession 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 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 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 make it possible to validate in molecular databases pest sequences from the flow of interceptions or entries.

In general, the LSV aims to ensure that the taxonomy skills used for its reference mission are maintained at a high level. 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 following recognition of its unique organisation obtained through the corresponding accreditation (ISO/CEI 17043 standard).

In Europe, this period will see the continuation of the H2020 VALITEST project, coordinated by the LSV's Reference Coordination Unit (UCR), which will produce validation data through two series of diagnostic test validation studies, including different combinations of pests/plants/matrices.

In addition, 2021 will see our activities expanded to include communication and training, within the framework of EURL mandates for fungi and oomycota, insects and mites, and plant-parasitic nematodes.

Research: gaining visibility

The LSV's analytical capacity will be maintained at a high level while it participates in research and development programmes that will provide the reference mission with knowledge and innovations.

To achieve this, the research questions addressed in responses to calls for tenders for national (ANR, CASDAR, Ecophyto, regional programmes), and European and international (H2020, PRIMA, 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 pests;
- the possible vector organisms 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 become operational: 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 and the mycology contracted unit with INRAE, and the DIAGEPITROP partnership with CIRAD.

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 supervisory ministries;
- 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,* 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 2020-21 will therefore include:

- validation by the laboratories of updated or innovative analytical methods for identifying and characterising regulated or emerging pests;
- joint coordination of the platform 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 methodology and research questions. It will capitalise 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 missions and an evolving context for plant health

The activities of the LSV will also be impacted by the introduction of new standards such as the new version of ISO/CEI 17025, and new European regulations, which will (i) result 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) 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.

➢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 aimed at developing or optimising 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 prior authorisation, issued on the basis of a dossier provided by the applicant, which should provide the information needed for a risk analysis. The LSV and the DEPR will continue to contribute to the development and interpretation of 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.

Issuing of marketing authorisations: facilitate the submission of applications, optimise their processing and allow 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 to implement processes and 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 strengthening 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 dossier management, by pursuing work on adapting the application forms used for plant protection products and fertilisers, proposing regulatory changes enabling dossiers to be uploaded, and continuing work on the D-Phy project to digitise dossier documents.

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 play an active part in the work under way on information systems dedicated to biocidal products (overhaul of the SIMMBAD tool and the helpdesk), and 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, 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 will continue to support the General Directorate, particularly with regard to the management measures proposed in the decisions.

Lastly, the department will continue the work initiated in 2018 on the comparative assessment of products containing glyphosate, by finalising decisions on MA renewal for the products concerned.

The DAMM will of course remain involved in the work of the platform for dialogue with stakeholders set up by ANSES in late 2017.

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 INRAE's CASPER USC (hosted at the Lyon Laboratory) 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 (UEs) 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. The CASPER USC is mainly involved in the cross-cutting strategic themes "Plant health" and "Epidemiology and surveillance". Secondarily, scientific issues and those related to surveillance of the topics addressed may find points of convergence with the "Antimicrobial resistance" strategic theme.

In a context where there are calls for a reduction in the quantity 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 2020-2021 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;
- 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;
- studying the effects of landscape and cropping practices on changes in the occurrence and frequency of resistance in pest populations.

The surveillance mission may also concern the unit in the context of phytopharmacovigilance (PPV, see below) and 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 for the benefit of 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 ANSES 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 seriousness 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 by MA holders to ANSES on the revenue from sales of PPPs.

For the period 2019-2021, the Agency has adopted a strategy for phytopharmacovigilance, broken down into five areas, which will provide overall guidance for its work:

1/ Collect signals: focus on increasing the number of relevant signals sent 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.

5. Occupational health

Background

Occupational health is in the spotlight now more than ever. The French National Assembly's Parliamentary Investigation Committee on occupational diseases and pathologies issued its report in July 2018 making several recommendations for improving the system of compensation for occupational diseases, improving the prevention system and supporting research. Along with the publication in late August 2018 of the report on the mission led by French MP Charlotte Lecocq on the evolution of the occupational risk prevention system and the report by Professor Paul Frimat on exposure to hazardous chemical agents, these various contributions will provide input for the discussions to be held between the government and the social partners on several subjects including occupational health. These discussions are likely to lead to significant, if not major, institutional changes. This provides the background to the orientations presented here, on the eve of preparation of a Fourth Occupational Health Plan, in which ANSES will play an active role. In a fresh approach compared to previous years, these orientations develop the main themes to be implemented on the topic of occupational health over the next three years, along with various actions that will be initiated or completed at the same time. They are based on the work programme sheets currently being finalised and are fully in line with the principles of ANSES's goals and performance contract (COP, 2018-2022).

Reinforce monitoring and vigilance work in order to anticipate emerging risks to workers as early as possible

The detection of emerging or re-emerging occupational health risks is a fundamental mission that relies on monitoring, research and vigilance work. Thus, while continuing its routine work in producing data and knowledge to support expert appraisal or developing tools for detecting emerging cases of new occupational diseases, the National Network for Monitoring and Prevention of Occupational Diseases (RNV3P) will hold discussions on optimising the scheme, taking better account of environmental diseases, and developing the occupational exposure thesaurus. On this last point, ANSES is now coordinating a working group bringing together the network's partners and occupational health stakeholders, whose work will help harmonise the coding of occupational exposures in order to improve 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 and phytopharmacovigilance (PPV), whose functions and collection methods differ but which are also used to identify emerging adverse effects on worker health. These vigilance data increasingly provide exposure information and reports of cases to supplement risk assessments. In accordance with the COP, work is being carried out to ensure the consistency and coordination of these vigilance schemes. It will help strengthen and improve each scheme's effectiveness in identifying relevant signals, particularly regarding the detection of emerging occupational diseases.

Contribute to improving risk control and prevention through the production of knowledge on hazards and exposure, and risk assessment

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 and are therefore key areas to be maintained in the coming years, especially in the field of occupational health. In line with the implementation of national plans and EU or French regulations on the assessment and management of chemical products, the Agency will provide scientific input to the authorities on the work described below.

First of all, the Agency will maintain a high level of support for the implementation of expert appraisals within a European regulatory framework **(CLP, REACh, PPPs, Biocides)**. 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 risk prevention and worker health 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.

With regard to **endocrine disruptors (EDs),** ANSES will continue its scientific support for national actions and plans for enhancing knowledge of exposure – particularly occupational exposure – to EDs. It will promote the French scientific position – aimed at regulating the substances of greatest concern – at EU level.

The Agency will also continue its work on **nanomaterials**. Improving knowledge of uses of and exposure to nanomaterials has a direct impact on the Agency's ability to manage and exploit the mass of data it oversees through the R-Nano register. As the organisation responsible for managing the register, ANSES intends to ensure that the quality and usefulness of the data contained in this database are assessed through detailed analyses and consultation with the various users. These data should also be used to document questions about emerging risks or specific industry sectors, linked for example to hazard alerts for certain substances or increases in specific uses. Work on this subject has already begun but needs to be stepped up. Lastly, the Agency will provide scientific and technical support to the authorities on harmonising the definition of nanomaterials in EU regulations. It will continue work on the feasibility of developing health reference values for nanoscale forms (TiO_2, etc.) and the assessment of substances in nanoscale form under REACh.

The identification and assessment of risks associated with **CMR** agents (carcinogens, mutagens and/or reprotoxic substances) will remain a major focus for the Agency, both as part of expert appraisals in response to formal requests and in the application of expertise to support chemical regulations (CLP, REACh, Biocides, PPPs, OELs). Besides a substance-by-substance approach, the objective and major challenge for the Agency in the coming years will be to develop new knowledge and robust methodologies to take into account the cocktail effects of chemicals, including CMRs. ANSES will have the opportunity to identify and test these scientific and methodological challenges in particular through the long-term study undertaken recently at the request of the Directorate General for Labour (DGT) to develop a method for classifying a mixture or process as "carcinogenic" under the 1993 Ministerial Order[16] and the drafting of a list of processes involving exposure to complex mixtures (e.g. those produced by welding fumes) that could be included in it. Following on from its expert appraisals on the identification and assessment of CMRs and its latest 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. A thorough examination of the need for greater coordination of ANSES's various work on substitution of hazardous products (CMR, PPPs, biocides) is necessary. It is important both at national level, where the role and coordination of the various parties involved in prevention should be clarified, and also at European level, where the European Chemicals Agency wishes to work with the Member States on this subject. Discussions on this subject may take place within the framework of the PST3's Action 1.10 on substitution, which is being led by the Agency.

With the recent signature of a memorandum of understanding with the DGT specifying the signatories' role and tasks in implementing the work programme on occupational exposure limits, the Agency will continue its scientific expert appraisal work with a view to making recommendations for atmospheric and biological limit values **(respectively OELs and BLVs)**, as well as its contribution to European work (ECHA). The challenge for the Agency lies in identifying priorities regarding the substances to be assessed in order to maximise the impact of its expert appraisals in terms of protection and risk 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 inhalation exposure route alone. The Agency will contribute to this debate as part of the work carried out for the PST4.

[16] Ministerial Order of 5 January 1993 listing the carcinogenic substances, preparations and processes within the meaning of the second paragraph of Article R.231-56 of the French Labour Code

The issue of **fibres, dust or particles** is a topic in which ANSES is particularly involved and on which it has produced a great deal of work in recent years. ANSES will continue devoting significant resources to this issue, besides the continuous production of methodological standards and the characterisation of particles in ambient air or workplace atmospheres. With regard to workers, the Agency will focus on studies to acquire knowledge on elongate mineral particles, for example, or on assessing the relevance of the particle size fractions used in "environmental health" and "occupational health" standards to characterise airborne particles. The publication of ANSES's expert appraisal on air pollution in underground railway areas has raised the question of the difference in risk management standards applied to the general population and to workers, the relevance and justification of this difference being increasingly challenged.

The Agency's work increasingly focuses on health effects related to **biological agents** or bioaerosols (e.g. mould, viruses, etc.), including a component on risks to workers. Recent work on the health impact of mould in buildings included a number of recommendations for prevention professionals. In addition, the conclusions and recommendations resulting from the Agency's work on risks to workers associated with climate change justify it devoting more attention to assessing the health risks of biological agents in the workplace in the coming years. It is all the more justified since scientific and technological developments related to the increasingly important role of biotechnology in our society raise questions about its consequences on the health of workers in this sector, a subject that is the focus of ongoing work at ANSES. Lastly, the health crisis due to the SARS-CoV-2 virus has shown the importance of strengthening work on biological risk related to occupational activities.

Assessing hazards and exposure to **electromagnetic fields** and their determinants is a subject still surrounded by scientific and societal controversy that justifies the Agency's continued involvement. Several expert reports have been published on the subject. These have highlighted growing concerns about exposure indicators and limit values, which are currently being reviewed by some international bodies. The Agency's experience and expertise on the subject argues for its involvement in the work, which could be carried out in association with other national or international bodies, with a view to adapting or developing exposure indicators that are relevant in view of the changes in uses and technologies, and proposing exposure limit values in line with the conclusions of the Agency's expert appraisals on the health effects of exposure to electromagnetic fields. This work also requires mapping the risks to workers associated with electromagnetic fields, which would help identify priorities for action. A formal request from the public authorities would enable ANSES to take on this work as a priority.

The extra-auditory effects of **noise** are becoming better known (diabetes, etc.) and may justify an update of the expert appraisal carried out by the Agency in 2013, especially on the methodology for assessing effects and in particular those related to interactions with other types of exposure (chemicals). The statistics on claims (accidents at work and occupational diseases) concerning hearing disorders among workers demonstrate the importance of developing knowledge and improving prevention in the workplace. A strong stance by the supervisory ministries through a formal request to the Agency would ensure that this work was given greater priority.

Lastly, ANSES will continue its work and discussions on the health risks associated with **organisational factors** by completing the second phase of its expert appraisal work on atypical working hours. It is clear that the development of new information and communication technologies and new forms of work organisation linked to the digitisation of the economy will lead to more knowledge and risk assessments being required as part of the public authorities' support for this development, which is liable to have harmful effects on worker health.

Continue developing complex expert appraisals involving multiple exposure situations in order to make progress on scientific and methodological issues

For the past few years, the Agency has had to conduct 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, the assessment of cumulative risks or **multiple exposure** 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 Agency is now beginning the second phase of work to assess the risks in the "household packaging" sector. A debate was recently initiated on the occupational health of workers in the cleaning and sanitation sector. These workers are subject to multiple risk factors, whether physical, organisational, biological or chemical. In addition, their medical monitoring is complicated by the job itself, often involving multiple sites and multiple employers. This debate led to the drafting of an internal request in 2019, whose first phase consists in identifying situations or populations that need to be investigated in greater depth. In the same vein, an expert appraisal recently began on the health consequences on flight crews of air pollution in airliners. The question of multiple exposure is consequently a major challenge for all those working in the field of occupational health and prevention. A challenge firstly with regard to knowledge of exposure, and then a methodological challenge for risk assessment. Moreover, it is highly likely that in the future this question will extend beyond the occupational environment by mobilising the concept of the exposome. It should be added that, in this respect, this question also represents an opportunity for the Agency to promote and exploit the integration of its various spheres of competence. We therefore still have a great deal of scientific and methodological progress to make in this area and that is why **this topic has become central** to the Agency's approach to occupational health issues. It is also part of Action 1.11 of the PST3[17] coordinated by the Agency, which will highlight the need to maintain this priority in the context of preparation for the PST4.

Ensure successful implementation of the new mission on expert appraisal prior to creation or modification of occupational disease tables

The reform of the workings of the Special Commission on Occupational Diseases of the Steering Committee on Working Conditions (COCT) provides for the outsourcing of the expert appraisal phase prior to creating or modifying an occupational disease table, to ANSES or any other agency offering similar guarantees with regard to the independence and robustness of the expert appraisal. For the Agency, this means carrying out work that it already routinely conducts as part of its normal missions. A working group on "Expert appraisals for occupational diseases" was set up in 2019 and published its first work in October 2020, including the methodology the group will use to conduct expert appraisals in response to formal requests. On this last point, in early 2021, ANSES will publish its first work on the link between pesticides (including chlordecone) and prostate cancer. The implementation of high-quality, reliable, independent collective expert appraisal based on a robust and proven methodology should help strengthen the scheme for recognising occupational diseases.

Strengthen the mobilisation and contribution of the human, social and economic sciences in expert appraisals relating to risks to workers

Assessing risks also requires the detailed characterisation of exposure, i.e. the **identification and understanding of its determinants**. It is therefore clear that an analysis of the actual work activity, closely linked to labour relations, economic imperatives, the organisation of production (subcontracting, etc.), the legal context and the wide variety of implicit and subjective representations, is necessary for a relevant assessment of uses and exposure, which are essential components of risk assessment. 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 context, which also plays a part in current and future exposure conditions, a sector analysis is also necessary and could call on different economic trends (e.g. industrial economics, innovation economics, labour economics). An understanding and a detailed analysis of the behaviour of stakeholders – whether consumers, workers or

[17] 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

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) need to be supported and developed. The aim will be to identify, as clearly and as early as possible in the work to be carried out in the field of occupational health, the nature of the issues to be addressed and the skills to be mobilised to tackle them, as was the case, for example, with the preliminary work on cleaning activities.

Work for better planning, coordination and visibility of occupational health research in France

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. ANSES's goals and performance contract (COP) requires the Agency to ensure that it gives greater visibility at national, European and international level to research in occupational (and environmental) health. In addition, the objective of Action 3.14 of the PST, led by ANSES, is to continue standardising and reinforcing the strategic planning behind occupational health research, particularly by strengthening the PNR EST through the consolidation of strategic planning. The Agency will therefore continue its discussions in this regard with the action's various partners and also with representatives of the major research funding programmes in France.

Strengthen European and international partnerships

ANSES has strengthened 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, RIVM, GR and TNO in the Netherlands[18], or in North America with NIOSH, INSPQ or IRSST[19]. These organisations are often consulted for contributions to expert appraisals, particularly on work undertaken or ongoing in the various countries. Relations with EU agencies (ECHA and EU-OSHA[20]) and international bodies such as the World Health Organisation (WHO) – particularly its Chemical Risk Assessment Network – should be continued, as well as participation in scientific networks such as MODERNET[21].

[18] 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)
[19] National Institute for Occupational Safety and Health (NIOSH), National Public Health Institute of Quebec (INSPQ), Robert-Sauvé Occupational Health and Safety Research Institute (IRSST)
[20] European Chemicals Agency (ECHA), European Agency for Safety and Health at Work (EU-OSHA)
[21] Monitoring Occupational Diseases and tracing new and Emerging Risks in a NETwork

III. Summary of the work programmes of the Scientific Divisions

1. *Research & Reference Division*
2. *Science for Expertise Division*
3. *Regulated Products Division*

1. 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 28 international mandates were held by these laboratories in 2020) 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 worksheets, which are discussed with the Agency's supervisory ministries. These sheets are now prepared once every two years and were therefore presented to the supervisory ministries in autumn 2020 for the period 2021-2022. They cover all the laboratories' reference, research, surveillance and expert appraisal activities, providing 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.

The purpose of this note is to highlight the **main orientations and highlights for 2021 contained in these 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 2021 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. More particularly, 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 2021, 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**. A wide-ranging debate will also be launched in 2021 in order to propose to the health authorities possible ways that the Agency may **streamline the work of organising inter-laboratory proficiency tests (ILPTs), on the basis of scientific and technical information**. 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 ILPT coordinators, to continue promoting sharing and the search for common solutions in work in this area. In view of the positive experience gained here in 2020, these events will take place online, if necessary, depending on the health situation.

In 2021, 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 finalise the acquisition and deployment of a **harmonised IT solution for managing the biological assets** of the Agency's laboratories.

Major sector-specific projects

The coming year will see continuation and completion of the measures decided but not yet implemented following the 2016 collective audit of the scientific activities of the Agency's laboratories (e.g. improving the visibility of our scientific output on the Agency's web pages), as well as **preparation of the teams for the next audit scheduled for late 2021**, according to conditions agreed upon in autumn 2020 in terms of the involvement of the High Council for Evaluation of Research and Higher Education (HCERES), and on the basis of the reference framework to be adopted before the end of 2020.

Scientific coordination for each of the six cross-cutting strategic themes (animal health and welfare, plant health, food safety, antimicrobial resistance, epidemiology and surveillance, exposure and toxicity of chemical contaminants) promoted by the six scientific directors will continue in 2021. 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, in view of the postponement of the internal seminar that had been planned for mid-2020 due to the COVID-19 context, various in-house workshops (organised in the form of webinars until the health situation again allows large gatherings of employees) will be offered in late 2020 and early 2021.

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. For example, 2021 will see the continuation of the projects selected in early 2020 as part of the **second internal call for expressions of interest for collaborative projects between Agency teams**; projects whose launch may have been significantly affected in the COVID-19 context of 2020.

In 2021, jointly with INRAE, CIRAD and VetAgro Sup, 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. It will also pay particular attention to the efficient implementation of the thesis projects that had to be extended due to the delay in activities linked to the health situation.

Lastly, in 2021, 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 2020 (remote) if required by the health situation. As well as promoting the scientific excellence of the Agency's entities – and especially its laboratories – on subjects of importance to ANSES, the objective is to promote 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 2021, 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. With the aim of promoting efficiency and streamlining internal processes as this activity develops, from 1 January 2021, the DSP will take over management of the intellectual property associated with the discoveries and innovations of the Agency's laboratories, a mission previously entrusted to the Legal Affairs Department.

Lastly, work will continue in 2021 to propose and deploy a **shared strategy on the more widespread use of whole genome sequencing (WGS)** in reference and surveillance activities. By adopting WGS and the associated innovative genomic techniques, the Agency will be able to carry out its diagnosis and surveillance activities faster, more efficiently and with increased robustness, in order to safeguard public health.

Communication and institutional relations

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 (INRAE, CIRAD, Ifremer, ACTA, etc.) and propose new structural partnerships, with the French Biodiversity Agency (OFB) in particular.

The DSP, and more especially 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 AllEnvi alliance, and will aim to consolidate its position in the Aviesan health alliance's bodies.

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. In particular, framework agreements to facilitate the exchange of biological materials and data will be finalised and deployed.

Europe and international

The DSP will be devoting significant efforts in 2021 to the forging of **European partnerships for the future Horizon Europe programme**. These will markedly shape the European research landscape in our fields of activity. Besides the partnership for assessment of risk from chemicals, which ANSES is lined up to coordinate, the DSP 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) **EJP co-fund on One Health** will continue in 2021. This partnership project, half of which is being funded by the European Commission, brings together 39 European human and animal health institutes from 19 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 European and International Affairs Department (DAEI), which is coordinating the project.

In 2021, with the support of the DAEI, the DSP will continue the internal scientific coordination of laboratories with European and international reference mandates (OIE, FAO and WHO) in order to define common priorities, share experiences and standardise practices.

Lastly, the DSP will continue to **manage the European Union Reference Centre 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.

1. Animal health and welfare theme

Animal health and welfare is an area of excellence of 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, 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 and their possible interactions with wildlife, 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' 2021 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 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 2021 implementation of these major strategic themes are highlighted here.

Strengthening our national and European positioning

The coming year will see the ramping up of the European Union Reference Centre (EURC) for the welfare of poultry and other small farmed animals, which ANSES is running with its Spanish, Italian and Danish partners. The first meeting of National Reference Centres in this field from the Member States of the EU took place in September 2020, and constitutes the foundation of a network of EURC partners. The Agency will continue its work with its European partners to set up a future European partnership on animal health and welfare in the framework of "Horizon Europe". If supported 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 2021 mainly characterised by the consequences of COVID-19

The Agency's research activities in 2020 were profoundly affected by the global health crisis, and the teams at ANSES were particularly proactive in making their coronavirus research expertise available to the scientific community and the State. The Agency's work 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 will undertake a programme of epidemiological investigation and methodological development 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, if selected. 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 2021.

Continuation of our research on major animal diseases

Continuation of the activities of the major experimental programme for surveillance of **low pathogenic avian influenza viruses**, especially within the fattened duck sector, should enable intervention studies to be set up in 2021 to identify effective measures to reduce the prevalence and cases of re-occurrence of these viruses.

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. 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. This work, which was interrupted in the spring of 2020 due to the health crisis, will be continued.

In order to respond to the emergence of outbreaks of **tick-borne encephalitis virus (TBEV)** 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.

Bovine tuberculosis, in both cattle and wildlife reservoirs, remains a major concern for our research teams and they will focus on developing vaccine strategies and reconstructing disease transmission trees in multi-host systems by integrating genomic and epidemiological data.

Therapeutic options and markers of infection of horses by **equine viral arteritis**, as well as the role played by mycoplasmas in equine respiratory diseases, will be explored in two university doctoral theses, which should lead to significant advances in knowledge on these two diseases.

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 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, 2021 will see the continuation of two ambitious projects on the **complex interactions between the different stress factors affecting honeybees** (PoshBee, H2020 programme) and on the development of air samplers to detect pesticides in bee colonies.
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 and the **OMAR network** (observatory for livestock mortality) will be progressively extended to cover most of the country, with support for these two networks from the DGAL.

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 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 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 offers 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 very recent entry into force of the **European Plant Health Regulation (EU) 2016/2031** has led to 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 will modify the scope of most of our national reference mandates and require skills to be reinforced on the pests that remain targeted by these mandates, as well as methodological developments that will be useful for their early detection and epidemiological surveillance. This will mainly be achieved through a reorientation of our study topics.

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

Lastly, **Regulation (EU) 2017/625 on official controls** has led the European Commission to set up new European Union Reference Laboratories (EURLs) in plant health; their activities started in 2019. Our three EURLs (plant-parasitic nematodes, insects and mites, fungi and oomycetes) will begin the second work programme of their first mandate. The main objectives of 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 *Xylella fastidiosa* and will also validate the method for identifying the bacterium's insect vectors, while supporting the 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 its 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 pursued. 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 corresponding EURL mandate.

At the same time, we will need to 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, an official method for its diagnosis on plants and seeds will be drawn up. 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 will still be paid to the *Bactrocera dorsalis* species complex. There will be a strong focus on this insect pest, mainly as part of EURL activities, and we will also 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 (EPPO and IPPC panels and working groups, H2020 VALITEST project, 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 under accreditation 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. 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 EFSA's horizon-scanning project, which has been extended for a further three years, an innovative methodology for monitoring the media and scientific literature will be pursued with a view to the 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 2021 see the continuation or launch of national and international collaborative projects (H2020 on the validation of diagnostic tests, EFSA on *Phyllosticta citricarpa*, ANR on phytoviruses, LabEx ARBRE on aerial dispersal of forest pathogenic fungi, CASDAR on apple leaf diseases and 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 one 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 will be the **NemAlliance cluster** (INRAE Centre Bretagne Normandie) for the study of plant-parasitic nematodes, the **Mycology contracted unit** (INRAE's ECODIV Department) for fungi and oomycetes affecting forest tree species, and the **DIAGEPITROP partnership via a research agreement** for our unit based on Reunion Island (CIRAD) concerning 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 even 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 2020.

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 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 2021, therefore, the laboratories will be able to implement complementary analytical methods as part of surveillance and control plans (*Listeria*, *Salmonella*, histamine, marine biotoxins), the Marine Strategy Framework Directive (MSFD), TDS3, the Biotox-Eaux network, or the surveillance networks led by the Agency (*Salmonella, Listeria* under development).

Lastly, **the surveillance platform for the food chain (SCA)** managed jointly by the DGAL and the DGS should provide support and drive the development of food safety monitoring and database management, in a spirit of unity among all the players involved. All of 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 foodborne illnesses**, with a strengthening of our ties and collaborative activities with the corresponding NRCs.

Technological and methodological innovations currently being deployed

One of the major objectives for 2021 will be to continue the roll-out of **whole genome sequencing** technologies (second- and third-generation technologies) begun in recent years and to deploy them more broadly for our reference activities and for the surveillance of microbiological contaminants, with a high level of responsiveness. This requires setting up an organisation linked to the Agency's **NGS and IdentyPath technology platforms** and suitable **bioinformatics** systems for data analysis and processing in support of the units. **Metagenomic approaches** will also be initiated in the framework of various research projects (META-DETECT, CARAVANE (transversality)).

The work initiated in this context concerns the use of MinION technology and is part of an in-house cross-functional project (Pathobiome, involving together numerous laboratories and the IdentyPath platform) designed to identify all pathogens on foodstuffs of plant origin using a metagenomic approach. This same platform is supporting the development of high-throughput qPCR technology for the molecular serotyping of *Salmonella* (GenoSalmo project) as an alternative to conventional serotyping, and for the serotyping and characterisation of *Listeria* (Genolisteria project). Once validated, it could become a method of choice for characterising these two major pathogens.

The deployment of MALDI-TOF mass spectrometry will continue within the platform; new approaches for strain characterisation will be studied in infrared spectrometry, while work using mass spectrometry to quantify staphylococcal enterotoxins and detect *Bacillus cereus* emetic toxins will continue**. Raman technology** will begin to be used as part of thesis work 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 developed, 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, will help strengthen partnerships with the various veterinary, food and public health institutes in the EU (Listadapt and ADONIS EJP projects). Some of these projects involve integrative, pivotal actions for the future, with the provision of reference materials and harmonisation of methodologies (TOX-Detect, CARE, HARMONY and MATRIX projects).

Training through research as part of doctoral studies and funded projects also enables partnerships to be forged, both in France (DIM ViPeRe, ANR Permali) and Europe (H2020 EuroBioTox, META-DETECT thesis topic with the BfR).

4. Antimicrobial resistance theme

Antimicrobial resistance is a major public health issue with a wide-ranging impact, involving issues of human and animal treatment, but also the 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 antimicrobial uses 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.

Strengthening the effectiveness of our surveillance schemes

From 2021 onwards, implementation of **regulatory analyses within the framework of the LNR's activities** will be stepped up, in line with changes in the European directives. It will remain 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 will now include *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[22] network and the Vigimyc[23] network for mycoplasmas). With regard to the RESAPATH network, structural changes will be finalised in 2021; these fall under Action 14 of Theme 3 of the EcoAntibio 2 plan. One aims to optimise data flows (EDIR Project, EcoAntibio) and allow the number of member laboratories to be extended, while the other will enable online consultation (R-Shiny) of these data. In addition, a Bayesian approach will be adopted to model RESAPATH data in order to characterise changes in the susceptibility of *Escherichia coli* clinical isolates to colistin (COBAYE Project, EcoAntibio).

Long-term monitoring of antimicrobial resistance will in 2021 also be supplemented by the implementation or completion of **specific surveys** in project mode (surveillance in fish farming, in the marine environment or in veterinary hospitals, antibiotic resistance of mycoplasma, 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 surveillance systems that currently exist in veterinary medicine within Europe and then studying the feasibility of longer-term generation of European data (Action 39 of the FIM).

Pursuing methodological developments for the detection of antimicrobial resistance

In 2021, the Agency will pursue several actions on **methodological approaches for monitoring antimicrobial resistance**. They include developing, assessing and validating phenotypic methods for determining susceptibility to antibiotics (IMPART project 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 study methods.

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 initiated (EcoAntibio 2) in 2021. This work will also be carried out or finalised as part of European or international projects such as TransComp-EST, the Joint Programming Initiative (JPIAMR), and both ARDIG and MEDVETKLEBS under the European Joint Programme on "One Health", etc. 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.

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

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 2021 (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 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, EcoAntibio projects). As a follow-up to the ANSES report on alternatives to antibiotics published in April 2018, work in 2021 will also focus on the relevance of credible alternatives to antibiotics (bacteriocins, algal hydrolysates, pre- and probiotics, phage therapy, vaccines) (RESPEC, CANIPHAGE, EVASION, EcoAntibio projects).

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

The laboratories are developing work on the subject 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 concerning the risks associated with antimicrobial resistance in environmental media initiated in 2018 by the Risk Assessment Department, whose conclusions will be issued in 2020 and which included a contribution from the ANSES laboratories, a new formal request will be added to the 2021 work programme on the **analysis of priority antimicrobial resistance risk profiles** (bacteria/resistance phenotype pairs) from the animal sector and of importance for public health. As part of ANSES's "Cross-functional" calls for expressions of interest led by the DSP, a project involving the laboratories and the Regulated Products Assessment Department will be completed in 2021 and will provide quantitative data on the development of antibiotic resistance in *Salmonella* after cleaning and disinfection of fattening facilities (QESABIO project, Fougères). Lastly, 2021 will see the continuation of the trans-disciplinary doctoral study combining the contribution of 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

The highlight in 2021 will be the start of work in support of the FAO under the **new mandate as FAO Reference Centre for antimicrobial resistance**, which was officially awarded to ANSES in autumn 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 2021 to conduct an inter-laboratory test on antimicrobial resistance in African countries, similar to what is done in the RESAPATH network. Other measures, including training, will also be discussed in 2021 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;
- participate in coordinating several surveillance schemes (RESAPATH, Vigimyc, *Salmonella*, RNOEA[24], Resumeq[25], 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, 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 increasing numbers of working groups;
- make a significant contribution to the production of articles for the *Bulletin Epidémiologique* on Animal Health & Nutrition published by ANSES-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 2021, **they will again offer major scientific and technical support to the supervisory authorities and carry out key research on Category 1 diseases** such as avian influenza, African swine fever (ASF), tuberculosis and brucellosis. In addition to this very important groundwork, ANSES's main orientations and significant epidemiological work for 2021 will focus on improving surveillance methods, better quantifying the role of wildlife in zoonoses, the impact of livestock farming systems and conditions on animal health and welfare, vector-borne diseases and methodological research. Lastly, and subject to funding, teams of epidemiologists from ANSES, together with their partners, will assess the circulation of SARS-CoV-2 and other coronaviruses in domestic and wild animal populations.

Improving surveillance methods

In a context where it is more vital than ever before to monitor health hazards for both food-chain safety and animal and plant health, there is a constant need to look for new ways to improve monitoring, including making 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.

Better quantification of the role of wildlife in zoonoses

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 conduct or 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. A new nationwide surveillance system for *Echinococcus multilocularis* in foxes will also be deployed.

[24] National network for epidemiological observation in poultry farming
[25] Equine mortality surveillance network

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

Criticisms of the livestock sector, and industrial 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 and pig 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. Among the animal husbandry conditions, there will be a focus on air quality in order to model the airborne spread of pathogens on both conventional and alternative farms.

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.

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*. Lastly, new machine learning and deep learning approaches will enhance the tools used for time series analysis, and methodological developments for optimised processing of large and complex data will be undertaken.

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). Looking ahead to the Horizon Europe programme, the development of a European Partnership for the Assessment of Risk from Chemicals (PARC) has been initiated and will lead to the creation of a European forum for cooperation between risk assessment entities and organisations in charge of research and reference activities. 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, and the preparation of research with our scientific partners to develop methods for analysing and characterising emerging hazards.

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 are also preparing 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 selective pressure of antibiotic residues from disinfectant biocides on antimicrobial resistance development (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 prepare the third total diet study (**TDS3**).

In the field of neurodegenerative diseases, in addition to the impact of co-exposure to certain pesticides on the development of Parkinson's disease, the Agency will develop a test for detecting this disease using the *in vitro* amplification of pathological alpha-synuclein, in order to contribute to its diagnosis in humans.

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.

In the area of metal studies, 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** will be 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 discussed, and addressed in the framework of the ANSES for Open Science strategy.

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

Research partnerships contribute to the generation of 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 vivo* fate (antibiotics, biocides, chlordecone), **mathematical modelling** (*in vitro-in vivo* extrapolation, physiology-based pharmacokinetic models).

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).

Strengthening our national and European positioning

Our laboratories and risk assessment units will be involved in several research programmes on chemical hazards supported at regional, national and European levels.

The establishment of the Horizon Europe programme is a great opportunity to strengthen cooperation in the area of chemical risk assessment. The new European Commission term of office and the Member States have proposed a European Green Deal to make the EU'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 framework, the establishment of a **European Partnership for the Assessment of Risk from Chemicals (PARC)** has been proposed. The Agency has lined itself up to coordinate this partnership, which will lead to the drafting of a strategic research and innovation agenda 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 risk assessment.

2. Science for Expertise Division

In line with the strategic orientations by thematic area for the 2019-2021 three-year cycle 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 a 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 respectively 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 ANSES's role, challenges and value, and integrating the Agency's work at European and international level. The choices have been made for their illustrative nature, as the Division's work is the result of the entire programme. In addition, for the communication and international parts, they highlight 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) or 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, with 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 the first component, particular attention will be paid to the mobilisation of our experts. Prolonged strikes and the health constraints resulting from the COVID-19 crisis led to long months during which collective expert appraisals were conducted through remote meetings. In addition, certain highly-publicised events in 2020 led to personal attacks on some experts, and in response the Agency initiated functional legal protection. Therefore, at a time when a new law on research is being adopted, **ANSES will be particularly supportive of its experts and their motivation for collective expert appraisal work**, through deployment of a dedicated internal quality process based on a new information system that was validated in October 2020.

In addition, many of the programme's sheets on methodological work make a direct contribution to improving the work's robustness: work on polluted sites and soils will continue, particularly as part of an update of the dedicated action plan to be prepared by a meeting of the Health Agencies' Strategic Coordination Committee in December 2020. Of course, central to this subject is the work of the ACCMER working group (Sheet 5.7.3), which is deploying the roadmap for support and implementation of the Scientific Board's recommendations, following completion of the work of the "Methodology of risk assessment" working group and its transposition into the expert appraisal reference framework.

Moreover, various planned or cross-cutting tasks particularly embody the desire for greater efficiency and robustness, namely:

- An **overall discussion on the health reference values** that ANSES is required to propose in its expert appraisal work. The central pillar of this debate will be the updating of the guide for developing TRVs (toxicity reference values, ANSES 2017), in order to integrate methodological developments in France as well as at European and international levels, and work on the homogeneity of approaches (especially in terms of the selected effects), and the data that can be used to establish exposure-response relationships. This approach also aims to advance work on multiple exposure, particularly in the context of mixtures in air (BTEX mixture, Sheet 5.5.6). Lastly, the variety of situations in which the results of ANSES work are used in risk management (ex-ante assessments before distribution/marketing, risk characterisation for ubiquitous contaminants, situations of polluted sites and soils, etc.) has led to the identification of a third component to this approach at the risk assessment/risk management interface: a component that warrants investigation to enable other risk stakeholders to make the best possible use of the Agency's work, including in areas where the reference values are not perceived in the same way (e.g. the area of nutrition/health with Sheet 7.1.1 on physical activity and sedentary behaviour).

- Work on data consolidation and interoperability: some of this is a continuation of the 2020 work programme (Ciqual/CONTAMINE interoperability, Sheet 1.7.6.), other activities result from work that was completed in 2020; this includes actions following the end of the cycle of formal requests from the inter-ministerial committee for the modernisation of public administration (CIMAP) or the internal request on the development of the CIQUAL system, which has defined a roadmap for future developments. This work also includes a joint debate with *Santé Publique France* to optimise facilities and resources for INCA/ESTEBAN (Sheet 1.6.3). These actions for 2021 should be viewed with a twofold perspective: on the one hand, the increasing difficulty of raising funding for updating data under budgetary constraints (see the financing round for TDS3, not yet finalised for Sheet 1.6.1, despite being clearly identified by the supervisory ministries) and, on the other hand, the launch of the "Green/Environmental Data Hub" action as part of the PNSE4.
- Continued alignment of the five vigilance schemes led by ANSES (veterinary pharmacovigilance, nutrivigilance, phytopharmacovigilance, toxicovigilance and the RNV3P), as well as the epidemiological surveillance schemes under the aegis of the **Vigilance Scheme Coordination Committee** (Sheet 9.2.1), which results from a milestone in Theme 2.1 of the COP. Particular highlights for 2021 will be the start of two new mandates for the groups supporting toxicovigilance and deliberations on the creation of a fourth group, with a more methodological scope, based on data quality and data mining. In terms of coordination, all these groups will now be coordinated by the Health Alerts & Vigilance Department, which will help standardise management.

  Lastly, the robustness or efficiency of other important Division activities will be further developed: **coordination of the National Research Programme for Environmental and Occupational Health (PNR EST)** (Sheet 10.3) will have to deal 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 SNPE2 or PNSE (transitioning from 3 to 4) increasingly stress the need to improve knowledge on risks. An important point will be securing permanent funds, and therefore maintaining the attractiveness of the programme. A broader debate is taking place with other research operators (and in particular the ANR) to increase the visibility of the PNR EST's offer, but also to avoid a situation where the project "selection rate" becomes a deterrent for research teams when compared with other sources of funding that are growing faster than that of the PNR EST. Of course, the Agency is well aware of the importance of keeping a system driven by questions arising from expert appraisal needs. The link with expert appraisals will therefore have to be strengthened, with better consideration of the recommendations of expert appraisals in the development of research questions. There is an ongoing debate about how to deal with the burden of a very large number of projects submitted, while ensuring the quality of follow-up of the selected projects (indicator 1.4 of the COP).

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 several projects related to the implementation of national plans or schemes:

As an extension of the report[26] produced as part of Action 1.5 of the goals and performance contract (COP), **the Agency plans to deploy a system for expert appraisal in socio-economic analysis** supported by the Social Sciences, Expertise & Society Unit (MiSSES). The increase in requests concerning the economic sciences addressed to ANSES, as well as the possible transfer of the missions of the High Council for Biotechnology (HCB), confirm 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. It will be progressively deployed according to three main pillars: establishment of an in-house team, creation of an expert committee specialised in socio-economic analyses, and development of a networking dynamic. A methodological reference framework will be designed that can be tailored to the various work themes, and these new skills will be applied to the Agency's various expert appraisals.

[26] "Socio-economic analysis: assessment and prospects for ANSES" scientific and technical support report, January 2020

In environmental health, 2021 will see the launch of the Fourth National Environment Health Action Plan (PNSE4). This launch was delayed due to the COVID-19 health crisis. Less broad in its coverage, this **new plan, which will be entitled "My environment, my health", will deal more selectively with a controlled number of subjects at the intersection of major health issues and strong societal expectations**, without duplicating what is being done by other ongoing plans. This is particularly the case for the SNPE2, which – for the Agency – needs to enter a more stable phase of substance assessment. For ANSES, mobilisation for the PNSE4 will take place – besides the environmental data issues described in Point 1.1 – through various projects in the field of nanomaterials, radiofrequencies, noise, and control of pests whose spread poses a threat to population health.

In the field of occupational health, 2021 will also see the preparation and launch of the fourth national occupational health plan. In particular, the Agency will enter the "production" phase of the scientific opinions that contribute to the creation or updating of occupational disease tables, following development of the methodology drawn up and published in autumn 2020. Two formal requests on the work programme are particularly symbolic in that **they go beyond the usual risk factors alone or in co-exposure, to investigate other forms of exposure likely to affect employee health**: this is Sheet 4.3.1 on the cleaning sector, which will examine closely the conditions under which the work of these professionals is organised and carried out, in addition to exposure to chemical and biological risk factors. There is also Sheet 4.3.2 on occupational health in the field of waste packaging recycling. One of the methodological challenges in the second phase of this internal request will be consideration of risks such as biological hazards and risks to the mental health of workers.

The question of identifying new "exposure functions" (other than the traditional quantities such as exposure time or quantity/dose incorporated) is not specific to the occupational health field, since it is also found in certain expert appraisals in environmental health, particularly for physical agents, through the 5G expert appraisal (see below) or the expert appraisal on the effects of new uses of NICTs (Sheet 5.4.1).

In food safety and nutrition, 2021 will see the actual start of work on one of ANSES's periodic reference studies carried out through the Division's "Methods and Observatories" field: **the third Total Diet Study (TDS3)**. Dialogue with the supervisory authorities on the substances was finalised in 2019 and led to the study's scientific scope and objectives being defined. The complexity and slowness of setting up the funding round for the study, whose deliverables are nevertheless expected in various national plans such as the SNPE2, has led the Agency to question the sustainability and model of funding for data acquisition in health-related expert appraisals, both in the area of food and beyond.

Furthermore, the Division considers that the following major projects should be started or completed, depending on the case, as part of the 2021 work programme:

- Completion of the expert appraisal in response to the formal request on 5G (Sheet 5.1.1);
- Launch of an expert appraisal to assess the health effect of reformulation scenarios concerning the nutritional composition of products after delivery of the Agency's response to the formal request on "thresholds" to the DGS and the DGAL (Sheet 1.4.6);
- Following the expert appraisal on antimicrobial resistance in the environment, launch of the response to a formal request on the risks of transmission of antimicrobial resistance from farm animals to humans (Sheet 2.2.6);
- Completion of the response to the formal request on the causality of adverse effects on farms due to the installation of wind turbines (Sheet 2.2.4);
- Finalisation of the assessment of the hazard associated with asbestos ingestion (Sheet 1.2.11). The deployment of "gold standard" methods to assess the weight of evidence led to real difficulties in the progression of this expert appraisal, which were compounded by the lack of available experts in the medical field during the COVID crisis. Beyond finalisation of the expert appraisal, the Agency will initiate a debate on the ways of deploying such methods, in conjunction with the ACCMER working group and the Scientific Board;
- Assessment of the risks associated with the consumption of nitrites and nitrates (Sheet 1.2.7).

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 objective 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 2021, and in the spirit of the SNPE2, this approach will also be deployed as part of Sheet 5.7.6 to investigate the existence of environmental determinants of growing chronic diseases such as obesity and diabetes.

With regard to phytopharmacovigilance (Sheet 5.2.6), the year's work will be guided by the objectives defined in the **PPV 2019-2021 strategy**, with particular attention being paid to characterising the signals to be reported by the partners and the launch of two major studies supported by the PPV: Pesti'loge, which is the pesticide measurement component of the second national housing campaign (CNL2), and Pesti'riv, the major study involving biomonitoring coupled with environmental measurements. The work programme will also include the follow-up to the national exploratory campaign to measure pesticides (CNEP) in air. 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. An update of the 2019-2021 strategy is also expected to be launched.

Close attention will be paid in 2021 to microbiological risk factors, and in particular Sheet 5.7.5. on aerosols, in order to develop a methodological framework for assessing health risks induced by biological agents found in air (or bioaerosols), where there is a lack of knowledge compared with the well-established framework for chemical agents. This situation was highlighted in particular during the collective expert appraisal work carried out on sewer workers; especially on their exposure to chemical or biological pollutants found in the air in sewers and, more recently, during the SARS-CoV-2 epidemic. It is very likely that this internal request will evolve, at least in part, through operational requests from various ministries, with discussions under way on underground railway areas and establishments open to the public. This work could fall under the umbrella of the PNSE4.

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), different worksheets in the field of vector control (Sheet 3.3.1 to 3) including the question of preventing resistance to control measures, and a sheet on prioritisation of health hazards affecting drinking water production originating from climate change (Sheet 3.4.4, an internal request). In the field of the *exposome*, ANSES will restart the work initiated with the Scientific Board in 2019 to determine the Agency's specific contribution through its different specialist activities, in particular that of expert appraisal in health risk assessment.

In terms of *responding to changes in consumer expectations and behaviour*, ANSES will work during 2021 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 a diet that excludes 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 the piloting of vegetarian menus). An internal request is also being prepared to provide a scientific framework for practices that are growing in response to societal demand for animal welfare labelling (Sheet 2.4.1).

Meeting societal expectations also means **initiating expert appraisals in response to formal requests from stakeholders**. In line with this, 2021 will see the continuation of the expert appraisal work initiated at the request of the *Robin des Bois* association on the problem of so-called "trash cows", while work under Sheet 4.2.2 should begin on air pollution along roadsides and associated risks for workers, primarily requested by the representatives of the personnel working on these road networks.

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**. In 2021, with regard to water-related risks, this will mainly concern assistance with the transposition into French law of the future European Directive on water, which will replace Directive 98/83/EC (Sheet 1.5.6), with a particular focus on changes in the framework for the expert appraisal on products in contact with drinking water (Sheet 1.5.2), for which ANSES is awaiting guidance from the DGS on the basis of its 2020 proposals. Publication of the report on its work registering tobacco products and the related scientific analyses will provide an opportunity to clarify ANSES's assessment strategy for this type of activity (Sheet 3.2.2). Lastly, work in 2020 also led to a tightening of the framework for action of ANSES's scientific and technical support to the DGS on funeral products (Sheet 3.2.3) by focusing it on the "regulatory guidelines" aspects. 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 (277 in 2019), which is a key point reflecting the mobilisation of scientific communities with regard to these emerging issues.

Support for developments and planning within the framework of the PNR EST will take form through firstly, the generation of stronger proposals in favour of "Open Science" and secondly, the formulation of research questions on the emergence of infectious diseases related to the environment.

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

These topics are generally addressed at Agency level, but some of the actions are managed by the Division's entities or call heavily on their resources, in accordance with the general orientations for this field. For 2021, this mainly involves the following:

- Various teams from the Division, especially the MiSSES, will be actively involved in rolling out the delayed (due to COVID-19) **international ANSES symposium on the credibility of scientific expertise and public decision-making, on the occasion of the Agency's 10th anniversary** (Sheet 8.2);
- Helping to increase **the visibility of the Agency's vigilance missions** (Sheet 9.2.2) through the now systematic translation of Vigil'Anses into English and by setting up a mini website and newsletter for this English version.

- Supporting and contributing to the in-depth reflection on risk information by the Department of Communication and Institutional Relations (DICORIS), in connection with the changes made to the editorial line of the website, social networks and the overhaul of the annual report. This reflection will focus mainly on the selection of subjects to be heavily promoted after the expert reports have been published, the choice of cross-cutting themes to be clarified, and the ways in which the results of expert appraisals become information;
- In conjunction with the DICORIS, continuing to promote PNR EST-funded work in forms appropriate to current health constraints, in order to maintain its visibility and attractiveness;
- Developing specific actions in favour of Open Science.

5. Europe and international

These actions are generally 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.

For the Division, this 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 entity at French level (with other partners such as SpF, INCa 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 2021, it is important to mention:

- Carrying out 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 large-scale project, for which ANSES is being lined up as coordinator, is expected to be the subject of a call for projects for the new cooperation tools ("partnerships") under the Horizon Europe programme[27];
- The submission and – if selected – launch of the last Horizon 2020 projects on emerging issues or those requiring innovation, such as exposure to chemical mixtures, a priority identified in the "European Green Deal" call under Horizon 2020.

And lastly, regarding work with the major European agencies:

- With EFSA, besides the continuation of existing cooperation, launch of a pivotal project to set up an advanced assessment system by a group of experts led and implemented by ANSES working partly for EFSA and its panel[28] in the framework of European regulations on food enzymes, in order to accelerate the creation and then updating of the positive list;

[27] Horizon Europe is the European Union's 9th framework programme for the funding of research and innovation, which will take over from Horizon 2020 on 1 January 2021 for a period of seven years (2021-2027)
[28] CEP Panel on Food Contact Materials, Enzymes and Processing Aids

- 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 comitology bodies (Sheet 5.2.12). In addition, the closeness of the Division's units to ECHA's teams also enables 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 (grouping of substances, etc.) and avoid investing significant efforts on legal action (aluminium salts, TiO_2, etc.).

3. Regulated Products Division

The 2021 work programme of the Regulated Products Division will be structured around the following objectives:

- Continue improving efficiency, particularly to reduce the time needed to examine MA applications for plant protection products (PPPs);
- Continue major projects initiated in 2020 (provide scientific support to the competent authorities in the context of permanent missions and formal requests);
- Evolve to address the challenges:
  - Facilitate the submission of dossiers and particularly the submission of applications for biocontrol products, and facilitate their examination;
  - Develop ways to improve knowledge and analyse the health and environmental impacts of regulated products, both before and after they are placed on the market;
- Strengthen information sharing and maintain listening and dialogue;
- Prepare for and adapt to European challenges in order to improve methodologies, assert its presence and reinforce its influence;
- Maintain and develop its international activity and presence to promote France's high standards.

1. Continuing to improving efficiency

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, the assessment of biocidal products, fertilisers and growing media, as well as the assessment of veterinary medicinal products.

An action plan to improve timeliness in examining MA applications for plant protection products was drawn up and implemented in 2017. The effect of these initial measures, particularly on the processing of the oldest dossiers and the simplification of processes, became apparent by late 2018 and should continue in 2021.

The French Agency for Veterinary Medicinal Products (ANMV) will also continue to improve its processes in order to achieve greater efficiency, in a context where the completion of Brexit significantly increased the number of applications and authorisations under its responsibility in 2020, and in order to prepare for the new European regulatory documents that will be implemented in 2022.

Information systems (IS) are essential to improving efficiency, and several strategic IS projects have come on stream in late 2020, such as D-PHY, a project to digitise the submission of applicants' dossiers, and VIGIE, a veterinary pharmacovigilance tool.

The D-PHY project has therefore been in a pilot phase since 2016 while its "claimed uses" component has been operational since 2018. It will be fully operational in late 2020 to digitise the submission of applications for plant protection products, and will be accessible to all firms in 2021. The VIGIE project, on a new veterinary pharmacovigilance tool shared with the ANMV and the Veterinary Pharmacovigilance Centre in Lyon (CPVL), will be launched in 2021 to supplement the electronic submission website for pharmacovigilance. Besides these two projects, work to fully digitise applications relating to MAs for veterinary medicinal products will continue in 2021, as will the ANMV's involvement in connecting up to European databases and repositories. At the same time, the division will continue to develop other IT tools (analysis of sales and usage data for veterinary medicinal products containing antimicrobials).

In the field of biocides, a study to modernise the information system used for managing the activity is being finalised. A call for tenders to select the service provider to develop the application was published in September 2020, for work to begin in 2021.

The MA Monitoring Committee, whose scope was extended to biocides in 2019, is continuing its work with regard to adaptation, feasibility and compliance of the risk management measures contained in the MAs. Concerning veterinary medicinal products, the Monitoring Committee (which was renewed in late 2019 for a further three years), will in 2021 continue the work begun during the first term of office and initiate new working themes.

2. Implementation of new key projects

ANSES will provide scientific support to the competent authorities, whether in the context of permanent missions or in response to formal requests.

In the area of surveillance and control, it regularly offers its expertise to State control bodies on plant protection products. It also carries out inspections of product formulation sites.

ANSES will provide its technical expertise in veterinary medicinal products to the Ministries of Health and Agriculture for preparation and adoption of the Order on adapting national provisions to EU law on veterinary medicinal products and medicated feed (Regulations No 2019/6 and No 2019/5).

The division will also help set up the Scientific and Technical Committee (CST), with the ministers having instructed INRAE, ANSES and the OFB to establish this committee within the Strategic Orientation Committee (COS) to ensure a clear and robust interpretation of the monitoring indicators but also to assess all or part of the plan and, if necessary, recommend changes to strengthen the policy to reduce the use of plant protection products.

ANSES will continue its assessment of SDHI fungicides throughout 2021, with the establishment of the "SDHI" working group 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 addition, in the first half of 2021 the Agency will finalise 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 the 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, will be completed during 2021 and will be followed by the launch of a second phase of work in 2021, also financed by ANSES.

In December 2017, as part of a plan by the French government to reduce the use of pesticides in farming, a CGAAER-CGEDD-IGAS inspection mission listed some of the active plant protection substances most frequently identified or mentioned in monitoring reports, which it described as giving cause for concern. The Agency then received a formal request to analyse the profile of these substances. In its opinion, ANSES undertook to update the risk assessments over the period 2020-2021, without waiting for re-examination of European approval of the active substances: firstly, the risk assessment for bystanders and residents of products containing prosulfocarb; and secondly, risk assessments for operators, workers, bystanders and residents of products containing the following substances: 8-hydroxyquinoline, ipconazole, flurochloridone, halosulfuron-methyl, spirodiclofen. The Agency will also assess the endocrine-disrupting effects of prochloraz on the basis of the European guidance document applicable since 2018.

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. Its opinion is expected in 2021.

The ANMV will continue its work on two major internal requests that have been occupying it since 2020: one 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; and the other on a review of knowledge on essential oils and plants of interest for herbal medicine and aromatherapy for food-producing animals.

It will continue to support various plans (EcoAntiobio2, Ecophyto, etc.), as well as public health policies on the prevention and control of arboviruses through its work on biocidal products used in vector control. A working group on this last theme was set up in 2020. In response to a formal request from the DGS, it will be responsible for supporting ANSES in proposing guidelines for monitoring insecticide resistance in mosquito vectors. The first results are expected in 2021.

3. Changes to address the challenges

a. Facilitate the marketing of biocontrol plant protection products

While respecting 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: tax reduced by between 50 and 95% depending on the nature of the products, applications submitted without delay, priority processing with the objective of minimising time to market.

On behalf of the Ministry of Agriculture, ANSES will continue to assess non-indigenous macro-organisms considered beneficial to plants; control methods that are also regarded as biocontrol solutions.

b. Develop ways to understand and analyse the health and environmental impacts of regulated products, both before and after they are placed on the market

ANSES will take part in numerous methodological projects and research programmes aimed at improving the assessment of regulated products. It will take pharmacovigilance signals and alerts into account.

For plant protection products and biocides, this work will cover aspects such as exposure scenarios and cumulative exposure, highly sensitising substances, setting MRLs in honey and hive products, pathogenicity of bacterial strains used in biocontrol, improved methods of assessing dietary exposure, and antimicrobial resistance.

For plant protection products, the contribution of studies and surveillance data collected under the phytopharmacovigilance scheme will be decisive, both for assessing active substances and plant protection products and for adapting MAs according to these results and data. The deployment in 2021 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, carried out among 1,000 to 1,400 residents and 500 to 700 non-residents, will make it possible to describe the exposure of residents living near agricultural crops to the pesticides used on these crops, in order to identify any overexposure and better understand how exposure occurs. Many sources of exposure will be explored (air, water, food, etc.).

In this field, and alongside the PestiRiv study, ANSES's work[29] 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

as well as on developing methodological tools for data mining.

ANSES will also continue its participation in the European human biomonitoring project HBM4EU.

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 poisoning cases related to all regulated products to be analysed and taken into account when issuing, amending or withdrawing marketing authorisations. In 2021, therefore, a report on cases of human exposure to plant protection products collected by poison control centres over the year 2018 should be available.

[29] See the DER's work programme

Lastly, in the field of veterinary medicinal products, the 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.

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.

The platform for dialogue on plant protection products facilitates exchanges 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. In 2021, 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.

Concerning information on biocides, as the Pesti'home study in particular has confirmed, it is essential to provide better information for the general public on the conditions for use of biocidal products. In 2020, ANSES therefore recommended measures to promote the proper use of biocidal products by the general public; some of these measures may be implemented in 2021.

With regard to veterinary medicinal products, ANSES will strengthen its national, European and international communication strategy, particularly with regard to stakeholders.

5. Prepare for and adapt to European challenges in order to improve methodologies, assert its presence and reinforce its influence

ANSES will support the competent authorities in preparing for meetings of representatives of the Member States at European and international level: PAFF Committee[30] and CCPR[31] for plant protection products, BPC[32], CG[33] and meetings of the competent authorities for biocidal products and the SCBP[34], participation in EPPO's[35] herbicide panel, and CVMP[36] and CMDv[37] for veterinary drugs. It will also provide support to the competent authorities in setting standards for fertilisers.

To better assert its point of view, ANSES will remain closely involved in European developments relating to methods for assessing the effectiveness and risks of regulated products.

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). For dossiers for which it is not the Member State, it will take 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 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.

[30] PAFF Committee: Standing Committee on Plants, Animals, Food and Feed at the European Commission
[31] CCPR: Codex Committee on Pesticide Residues
[32] BPC: Biocidal Products Committee of ECHA (European Chemicals Agency)
[33] CG: Coordination Group for Biocidal Products, for which ECHA provides the secretariat
[34] SCBP: Standing Committee on Biocidal Products
[35] EPPO: European and Mediterranean Plant Protection Organisation
[36] CVMP: Committee for Veterinary Medicinal Products, within the European Medicines Agency
[37] 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 presence 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 investment in the network of HMA agency heads.

A new European strategy for the EMA and the network of agencies (HMA) will come 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 early 2020, the ANMV set up a new organisation to ensure it was better placed to meet the Agency's challenges for the coming years in the context of the ongoing European regulatory changes. In 2021 it will draw up a new 2022-2026 roadmap taking into account all the strategic orientations defined at both national and European level.

In addition, the 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 the EMA and the European Commission for discussions on the implementation of the new information systems needed.

6. Maintain and develop its international activity and presence to promote France's high standards

Our international activities have been heavily impacted by the current international health context.
However, through its mandate as an OIE Collaborating Centre in the field of veterinary medicinal products, the ANMV will continue its deep commitment to combating antimicrobial resistance, in particular by setting up the OIE database and training national focal points.

It will also do its best to continue providing assistance with development and sharing French expertise through the various cooperation agreements signed with its partners worldwide (China, Thailand, Ukraine, Saudi Arabia), and will try to make exchanges with Russia a reality.