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

Investigate, evaluate, protect

2019 ANNUAL REPORT

PLANT PROTECTION PRODUCTS, FERTILISERS, GROWING MEDIA, ADJUVANTS AND BIOCIDAL PRODUCTS

Review of ANSES's 2019 activities in assessing products, issuing marketing authorisations and permits, and phytopharmacovigilance

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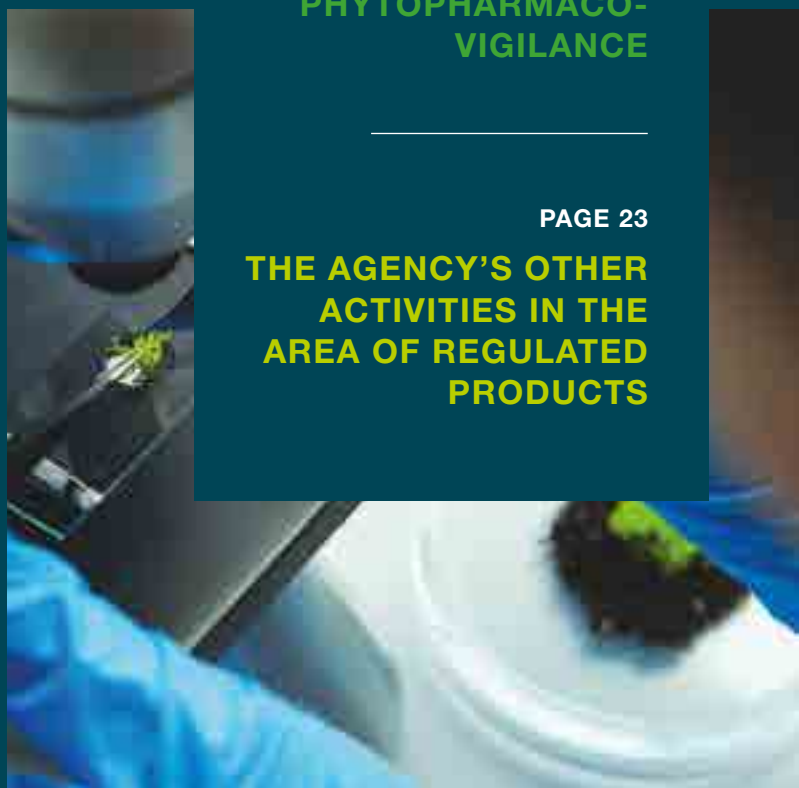


Introduction

Under Article L. 1313-3-1 of the French Public Health Code, the French Agency for Food, Environmental and Occupational Health & Safety prepares a report each year, addressed to Parliament, giving an account of its activities, in the framework of:

1. its missions relating to plant protection products, adjuvants, fertilisers and growing media, laid down in the tenth paragraph of Article L. 1313-1;

2. its risk monitoring missions, in particular as part of the phytopharmacovigilance scheme, laid down in Article L. 253-8-1 of the French Rural and Maritime Fishing Code;

3. its missions relating to biocidal products, laid down in the eleventh paragraph of Article L. 1313-1.

After a brief reminder of the principles that frame ANSES's work in the area of plant protection and biocidal products, fertilisers and growing media, and of the procedures for assessing and issuing marketing authorisations (MAs) for these products, this report presents the work conducted by the Agency on this topic in 2019, including in the area of phytopharmacovigilance.

ANSES's sphere of competence is vast, since in addition to food safety, it is responsible for risks in the areas of environmental and occupational health, human health, animal health and welfare, and plant health. It therefore works on microbiological, chemical and physical risks.

In 2015, the Agency was entrusted with establishing a phytopharmacovigilance scheme, and with granting, amending and withdrawing marketing authorisations (MAs) for plant protection products, fertilisers and growing media. In 2016, this responsibility was extended to MAs for biocidal products.

At ANSES, the risks and effectiveness of plant protection and biocidal active substances and products are assessed both before and at the time the products are placed on the market, or through post-authorisation monitoring of their impact. This assessment is part of a comprehensive approach that is inseparable from the monitoring of these substances' residues in food and the environment and, more broadly, their impact on health, the environment and biodiversity.

The principles that frame ANSES's work in the area of plant protection products, fertilisers, growing media, adjuvants and biocidal products

ANSES exercises its missions in the area of plant protection products and biocides, adjuvants, fertilisers and growing media in compliance with the European and national regulatory frameworks, and while guaranteeing application of the following principles:

→ **the independence and rigour of ANSES's scientific expert appraisals, as well as the functional separation of assessment and management**. The Regulated Products Assessment Department (DEPR) assesses the hazards and risks of products to humans, animals or the environment, and also assesses their effectiveness. The Market Authorisations Department (DAMM) receives application dossiers and examines their admissibility, and reviews marketing authorisation decisions and permits. A Managing Director General coordinates this work and ensures that it is in step with the monitoring and vigilance activities mentioned in the next point;

→ **a strengthened capacity for detecting warning signals and alerts relating to any adverse effects or non-compliance of these products**, in particular through implementation of the phytopharmacovigilance scheme, coordination with the toxicovigilance scheme – which is also coordinated by ANSES – and resources for inspection and control;

→ **an ability to fund independent studies** in the framework of phytopharmacovigilance, through a tax on plant protection products, or more broadly in the context of the scientific and technical research programmes funded by ANSES.

All of these activities are subject to ISO 9001 certification – renewed at the end of 2019 – and form part of a dedicated process that was radically overhauled in 2019 when ANSES's process and risk maps were revised. These activities are therefore covered by a quality process that guarantees traceability, takes risks into account and ensures management based on indicators.

In the interests of transparency regarding the decisions taken, all acts are published on the Agency's website, along with the findings of the assessment on which they are based.

The information contained in the product MA decisions is also consolidated on the E-Phy website (https://ephy.anses.fr), which is an updated catalogue of products and their conditions of use.

For biocides, the list of products authorised in Europe in accordance with Regulation (EU) No 528/2012 is available on the Register for Biocidal Products managed by ECHA via the R4BP platform.

Dossier assessment activities

FOUR TYPES OF PRODUCTS TO BE ASSESSED AND THE SAME NUMBER OF REGULATORY FRAMEWORKS

The Regulated Products Assessment Department (DEPR) is responsible for the following tasks, within the framework of European and national regulations:

→ assessment of the hazards and risks to humans, animals or the environment, as well as the agronomic benefits, of plant protection substances and products (Regulation (EC) No 1107/2009);

→ assessment of the hazards and risks to humans, animals or the environment, as well as the effectiveness, of biocidal substances and products (Regulation (EC) No 528/2012);

→ assessment of fertilisers, adjuvants for fertilisers and growing media, in accordance with the provisions of the French Rural and Maritime Fishing Code, and in the context of European Regulation (EC) No 2003/2003.

→ Lastly, non-indigenous macro-organisms beneficial to plants and introduced into the environment are also assessed by the DEPR in accordance with the provisions of the French Rural and Maritime Fishing Code.

The general purpose of these regulations is to ensure a high level of protection for humans, animals and the environment by only placing on the market those products that are effective and do not have adverse effects on human health or entail unacceptable risks for the environment and the organisms it harbours.

For plant protection products and biocides:

→ active substances are assessed at European level, leading to an approval regulation if the active substance fulfils the conditions for approval of the European regulations. The European Commission has drawn up a positive list of active substances approved at EU level;

→ once the active substance(s) they contain have been approved, products undergo a zonal[1] or EU assessment prior to national marketing authorisation being granted.

[1] Under Regulation (EC) No 1107/2009, Europe has been divided into three zones: north, centre and south, within which Member States can rely on an assessment carried out by another Member State (Rapporteur Member State) to authorise a product used outdoors. For products used under shelter, the assessment may be shared throughout the EU.

ASSESSMENT OF ACTIVE SUBSTANCES

Active substances are assessed from three angles:

→ assessment of the hazard intrinsic to the active substance;

→ assessment of exposure and of the risks resulting from this exposure under the proposed conditions of use, to humans and the environment, for one or more representative uses;

→ assessment of the substance's effectiveness.

Approval of **plant protection active substances**, whether they are micro-biological, chemical, synthetic or natural, falls within the remit of the EU, following an opinion by the European Food Safety Authority (EFSA). ANSES participates in the assessment of these substances, as a Rapporteur Member State, in the framework of EFSA's work. The timetable for the re-examinations and the distribution of the substances to be assessed between the various Member States are decided at EU level.

The EU also has competence for the approval of **biocidal active substances**, which is granted after an opinion by the European Chemicals Agency (ECHA). The biocidal active substance can be a chemical compound or derived from a micro-organism exercising its biocidal action on or against harmful organisms. Moreover, in the field of biocides, there are 22 types of biocidal products, divided into four groups:

→ disinfectants (human or animal hygiene, disinfection of surfaces, disinfection of drinking water, etc.);

→ preservatives (for products during storage, for wood or construction materials, etc.);

→ pest-control products (rodenticides, insecticides, repellents, etc.),

→ other biocidal products (embalming fluids, antifouling products, etc.).

Approval of a biocidal active substance is established for one or more product types. The assessment therefore focuses on an active substance-product type combination, and assesses the risks and effectiveness for representative uses of the product type concerned.

ANSES participates as a Rapporteur Member State in the assessment of biocidal and plant protection active substances, in the framework of the EU assessment of dossiers. ANSES also takes an active part in the comment phase and in discussions of the draft assessment reports submitted by the other Member States and, for biocides, in the drafting of opinions by ECHA's Biocidal Products Committee (BPC).

SCIENTIFIC ASSESSMENT OF MARKETING AUTHORISATION APPLICATIONS

The assessment of applications for plant protection products, biocidal products, fertilisers and growing media relies on a scientific examination of the dossier, which is essentially carried out at European, zonal or national level depending on the regulations concerned. It consists of a thorough review of the product's physico-chemical properties, the risks to human health, fauna, flora and different environmental media, as well as an assessment of the product's effectiveness.

This assessment is based on the dossier provided by the applicant, which includes the studies required by the regulations and relevant scientific publications, if available. In addition, for MA renewals, observation data is needed on the impact of these products, collected as part of the phytopharmacovigilance scheme. The findings of the assessment are then presented to an expert committee (CES).

These expert committees are made up of independent external individuals who responded to a call for applications and were selected by ANSES – after an analysis of their personal connections and interests – for their recognised skills in the scientific fields mobilised for the assessment (toxicology, ecotoxicology, chemistry, exposure assessment, risk assessment, agronomy, entomology, microbiology, etc.).

Several expert committees, each specific to a substance or product type, contributed to ANSES's assessment work in 2019, a year during which the mandates and composition of these committees were renewed:

→ The CES on *Plant protection products: chemical substances and preparations* and the CES on *Micro-organisms and macro-organisms beneficial to plants*, whose scope was revised slightly when they were renewed, to form the CES on *Plant protection products and biocontrol*, which has been partnered with a permanent working group on "Macro-organisms beneficial to plants";

→ The CES on *Fertilisers and growing media*;

→ The CES on *Biocidal substances and products*.

The assessment findings (in French), published on the Agency's website, summarise the results concerning the hazards (including a toxicological classification for human health and the environment) and risks to humans, animals or the environment, as well as the effectiveness of the products in question for the claimed uses. The conditions of use for which the assessment has been carried out are also specified (doses, conditions of application, targets, etc.).

IMPLEMENTATION OF METHODOLOGICAL DEVELOPMENTS AND PRODUCTION OF USEFUL DATA FOR THE ASSESSMENT

The Agency's scientists working to assess plant protection products, fertilisers and biocides are involved in a wide range of activities aimed at developing or optimising assessment methodologies, as well as drafting and updating harmonised guidelines for the examination of dossiers in accordance with European regulations. This work is most often undertaken in partnership with other organisations or as part of national, European or international working groups. Its purpose is not only to improve the interpretation of assays performed to determine chemical hazards, but also to construct detailed exposure scenarios and models for use in assessing hypothetical risks and agronomic benefits.

When carrying out its assessment missions, in addition to the information found in the dossiers submitted by the applicants, ANSES may identify additional data needed for effectively conducting the assessment of certain dossiers, or for proposing changes to assessment methods and practices.

These data most frequently concern environmental contamination, human exposure to the products concerned, or the risks to humans and the environment associated with product uses. The Agency can also fund specific studies to encourage the production of new knowledge needed for its expert appraisals. For example, ANSES issued a call for tenders for carrying out several toxicology studies in order to improve knowledge of glyphosate (see box in Section 9). Some of these studies, dealing with the adverse effects of the products concerned, are made possible thanks to the financing put in place as part of the phytopharmacovigilance scheme (see Section 8), while others fall within the general framework of the scientific and technical research programmes funded by ANSES.

In order to conduct the assessment correctly, ANSES may need to obtain additional data: environmental contamination, human exposure to the products in question, and risks to humans and the environment linked to product use.

Activities in issuing, amending and withdrawing product marketing authorisations

ACTIVITIES RELATING TO PLANT PROTECTION PRODUCTS, FERTILISERS AND GROWING MEDIA

Decisions regarding the issuing, amendment and withdrawal of marketing authorisations are examined by the Market Authorisations Department (DAMM) and submitted to ANSES's General Directorate for a final ruling.

As the interface with applicants, the DAMM is in charge of receiving applications and dossiers, and reviewing decisions on marketing authorisations and permits related to these products. It rules on their admissibility and provides information that helps place the applications in context: agronomic context and conditions of use of the products, as well as analytical information for the comparative assessment of products in application of Article 50 of Regulation (EC) No 1107/2009, for the submission of dossiers concerning active substances that are candidates for substitution.

The DAMM also examines applications for experimentation permits and manages declarations of product trials and experiments, using the dedicated SIDEP online reporting service, both before tests have been set up and after experiments have been established, within the framework of officially recognised trials.

With the examination of parallel trade permits, the DAMM acts as the interface with other Member States for the transmission of information needed for this examination, as well as for updating the list of products whose introduction is authorised for personal use, in application of Article R. 253-27 of the French Rural and Maritime Fishing Code.

Decisions relating to marketing authorisations (authorisation, amendment, refusal or withdrawal) and permits are reviewed taking into account the results of the scientific assessment, the agronomic context in which the product is used, and/or the existence and characteristics of other products available on the market.

ACTIVITIES RELATING TO BIOCIDAL PRODUCTS

Since July 2016, ANSES has also been responsible for issuing, withdrawing and amending MAs for biocidal products, in accordance with European Regulation (EU) 528/2012, on the basis of a scientific assessment of their effectiveness and risks. The Agency also has responsibility for declarations to the biocidal products inventory (SIMMBAD).

The organisation put into place takes into account the specific features of the European regulations governing biocidal products while guaranteeing the independence of the assessment and at the same time safeguarding the Agency's ability to effectively support its positions in assessment and management in the framework of the European procedure. This is because biocidal products have certain specific features that impact ANSES's organisation and work in examining these dossiers:

→ a very broad field of products and uses;

→ very tight regulatory deadlines;

→ a European procedure that simultaneously addresses issues relating to assessment and management, and in which mutual recognition is predominant. Great importance is thus attached to the collegial review of dossiers between Member States, and efforts are systematically made to harmonise conditions of use and management measures before the decision is made.

THE MARKETING AUTHORISATIONS MONITORING COMMITTEE: SUPPORT FOR DECISION-MAKING

When reviewing decisions relating to marketing authorisations, the Agency's Director General may call on the Marketing Authorisations Monitoring Committee, set up to deal with plant protection products from 2015 and biocidal products from 2019.

The Director General may consult the Committee on the conditions under which the marketing authorisations will be implemented (Art. L. 1313-6-1 of the Public Health Code); minutes of any meetings are published on the Agency's website.

The Monitoring Committee was convened five times in 2019.

In the area of plant protection products, it examined questions relating to the applicability of bee protection measures depending on the flowering period, the comparative assessment of products, with the specific case of the use of glyphosate-based products in viticulture, the situation of metazachlor and groundwater, and risk management measures for protecting residents and bystanders (no-spray zones for residents).

The MA Monitoring Committee also issued its opinion on various topics relating to the use of biocidal products, in particular, conditions of disinfectant use in hospitals, use of permethrin to impregnate textiles for vector control purposes, and the revision of the conditions of authorisation of certain rodenticide products to limit the poisoning of pets.

INSPECTION AND CONTROL OF PLANT PROTECTION PRODUCTS, FERTILISERS AND GROWING MEDIA

The Agency has an inspection mission with regard to the production, formulation, packaging and labelling of plant protection products, adjuvants, fertilisers and growing media.

These activities are carried out under a memorandum of understanding signed in 2015 between the Directorate General for Food (DGAL), the Directorate General for Competition, Consumer Affairs and Fraud Control (DGCCRF) and ANSES, in order to ensure that the different inspection and control bodies under these administrations and ANSES work in a coordinated manner, with exchanges of information on annual plans and their reviews, but also on the establishments visited, in conjunction with the regional food services (SRALs) of the regional directorates for food, agriculture and forestry (DRAAFs) and the departmental directorates for the protection of populations (DDPP). The aim here is to avoid successive controls by multiple inspection bodies.

The work focuses on formulation/packaging/labelling establishments, with a view to checking the traceability of product composition and formulation, post-production labelling, and the implementation of new verification methodologies. There have been numerous interdepartmental exchanges with the protocol signatories, as well as with the Directorate General for Customs and Indirect Taxation and the DGAL's National Brigade for Veterinary and Phytosanitary Investigation, including sharing of information relating to decisions, conditions of use, product uses and labelling, as well as contributions in the context of requisitions.

ANSES'S WORK IN THE AREA OF PLANT PROTECTION PRODUCTS, FERTILISERS AND GROWING MEDIA IN 2019

The high level of activity was sustained in the fourth full calendar year following the transfer to ANSES of competence for MAs and permits for plant protection products, fertilisers and growing media, with the receipt of:

→ 372 applications relating to dossiers for active substances[2];

→ 2,023 applications relating to marketing authorisations or permits, of which 221 involved fertilisers and growing media, 15 adjuvants, and 1,787 plant protection products. The latter included:

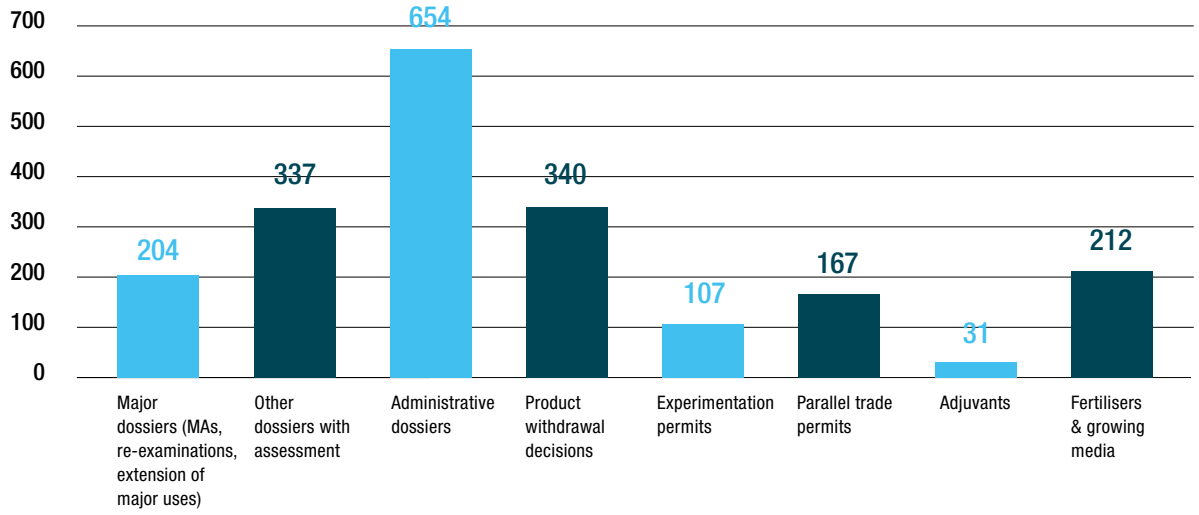
- 190 dossiers regarded as "major" (new MAs, renewal of MAs or extension of major uses);
- 797 administrative applications;
- 130 experimentation permits;
- 187 parallel trade permits;
- 483 other applications subject to scientific assessment.

→ More than 2,000 decisions were signed, of which 212 concerned fertilisers and growing media, 31 adjuvants and 1,809 (88% of the total) plant protection products. The latter included:

- 204 decisions corresponding to dossiers regarded as "major", including renewals of authorisations restricting uses;
- 654 administrative decisions;
- 340 decisions to withdraw products from the market, including products containing active substances reaching the end of their approval, the withdrawal of glyphosate-based[3] products, and the withdrawal of all epoxiconazole-based products following ANSES's opinion on the endocrine-disrupting nature of the active substance epoxiconazole[4];
- 107 decisions on experimentation permits;
- 167 decisions on parallel trade permits;
- 337 other authorisation decisions subject to scientific assessment.

Decisions to withdraw products from the market accounted for 17% of all decisions in 2019. However, it should be noted that among the decisions relating to dossiers regarded as "major", some may lead to restrictions on use.

Number of decisions taken in 2019 according to the type of application



[2] This concerned all types of dossiers relating to active substances: amendments, classifications, confirmatory data, MRLs, new substances, renewals, specifications, administrative amendments, etc.

[3] News update of 9 December 2019, *ANSES announces the withdrawal of 36 products containing glyphosate*

[4] ANSES Opinion on the endocrine-disrupting nature of epoxiconazole (19 April 2019, published 28 May 2019)

Moreover, as part of efforts to **simplify procedures for users**, the D-Phy project to digitise applications continued, with the aim being a launch in early 2021. This is a major opportunity for ANSES to improve efficiency; it is expected to save time on data entry and improve the reliability of data collection, contributing to a reduction in processing times.

Lastly, ANSES continued its extensive work in **assessing plant protection active substances**, illustrated by the figures in the table below. This activity concerns previously authorised substances that have to be re-assessed before their approval can be renewed, or new substances that have to undergo an assessment with a view to obtaining a first approval.

ANSES's work in assessing plant protection active substances – Number of dossiers processed, by category (2015-2019)

	2015	2016	2017	2018	2019
Dossiers submitted – RMS	10 (4 micro-organisms)	4 (0 micro-organism)	2 (1 micro-organism)	6 (2 micro-organisms)	1 (0 micro-organism)
Dossiers submitted – Co-RMS	7	6	0	10 (0 micro-organism)	0
Finalised assessment reports – RMS	7 (2 micro-organisms)	6	10	13 (1 micro-organism)	10 (1 micro-organism)
Finalised assessment reports – Co-RMS	5	5	12	13 (2 micro-organisms)	8 (3 micro-organisms)
Indicators of activity for the substances	29	21	24	42	19

RMS: Rapporteur Member State

In 2019, ANSES continued its efforts to facilitate the marketing of biocontrol products

In order to develop access to the market for biocontrol products, a certain amount of latitude is granted for applications concerning plant protection products meeting the criteria for biocontrol products referred to in Article L253-6 of the French Rural and Maritime Fishing Code. These applications are therefore dealt with immediately and benefit from a lower tax rate, half the normal processing time for new authorisations, and priority examination at each stage.

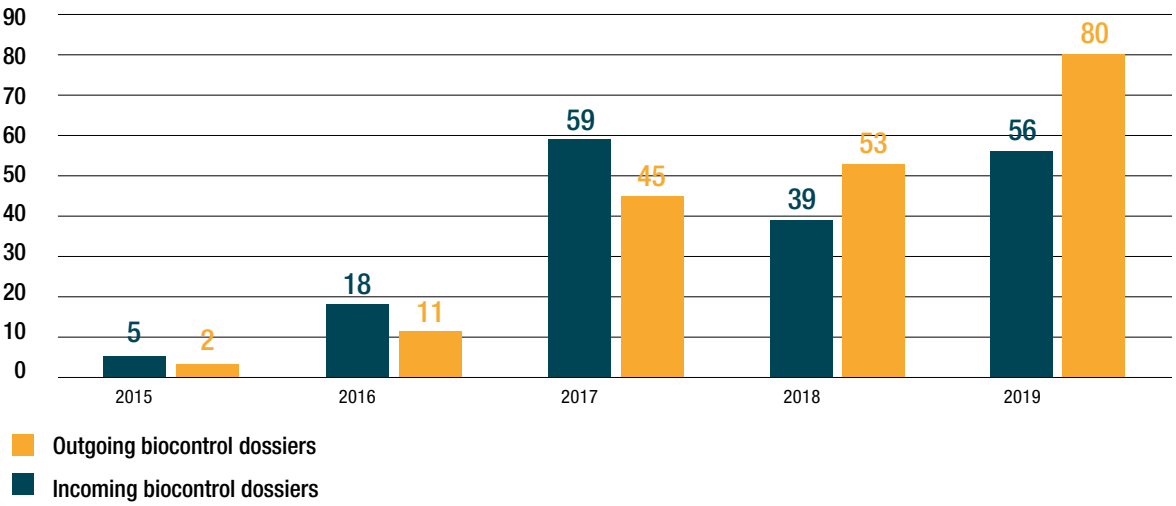
In 2019, among the dossiers identified on submission as relating to biocontrol:

→ 11 applications for macro-organisms, not covered by the plant protection regulations, were received;

→ 56 applications for MAs and new uses (first MAs, MAs by mutual recognition, generic products, extensions of major use) were received;

→ 80 decisions were taken on new MAs and new uses, compared to 53 in 2018, representing an increase of over 50% in the number of decisions issued.

Number of incoming/outgoing biocontrol dossiers: new MAs and new uses



The sharp increase in incoming biocontrol dossiers observed between 2016 and 2017 is linked to the growth of the biocontrol field in 2017.

Improving information and dialogue with stakeholders

In 2019, ANSES continued its efforts to improve information and dialogue in its activities relating to plant protection products, fertilisers and growing media.

The **platform for dialogue with stakeholders**, set up in 2018 to ensure regular communication with all stakeholders and chaired by Bernard Chevassus-au-Louis, continued its activity with two plenary discussion meetings in March and October. These meetings, which took place in an atmosphere of productive, constructive dialogue, each brought together some 50 participants representing all the stakeholders.

In 2019, in addition to topical issues, the following themes were addressed:

→ Decision framework: uniform principles for assessment and authorisation of plant protection products;

→ Methodology for the development and application of guidance documents;

→ Categories of substances (natural, chemical, low-risk, low concern, usable in organic farming, etc.) and product types;

→ MA Monitoring Committee activities;

→ Pesti'Home study;

→ Changes to the regulatory provisions aiming to protect domestic bees and wild pollinating insects;

→ A four-year review of MA activities.

Management of the **E-Phy website** has been improved, with news regularly updated, in particular on the conditions for withdrawing products from the market, handling of information requests as they are received and verification of error reports. Training has also been organised for interested users.

The file of information on MAs, **available as open data** on the data.gouv.fr website, also evolved, offering new information that had been requested by users.

In addition, in order to improve the dissemination of information on MAs, and in addition to the decision register and the E-Phy website, in late 2018 ANSES launched a **monthly MA bulletin**, which provides easy access to the decisions taken by the Agency. In December 2019, an **issue devoted to fertilisers** was published.

The file of information on MAs are available as open data on the data.gouv.fr website

ANSES's work in the area of biocidal active substances and products in 2019

The number of applications for biocidal products remained broadly stable in 2019. The number of application dossiers for which France was the reference Member State increased significantly, partly due to the departure of the UK authorities, which are no longer able to assess cases. Most applications received in 2019 concerned disinfectant products, in particular those based on sodium hypochlorite or lactic acid, which were mainly grouped into families of biocidal products.

Number of applications relating to biocidal products in accordance with Regulation (EU) No 528/2012 received by ANSES in 2018 and 2019

Application type	Number in 2018	Number in 2019
First MA: initial application	23	36
First MA: minor/major change	57	45
Mutual recognition	75	45
Administrative applications	150	124
Other: R&D notifications, provisional MAs	36	29
Renewal dossiers	28	28
Total	**369**	**307**

Activity regarding the issuing of marketing authorisations declined compared to 2018. In 2019, ANSES issued 300 decisions for biocidal products. This included 86 relating to a first MA, major change or mutual recognition (compared with 110 in 2018). However, while the overall number of decisions was lower, it covered a large number of biocidal products: more than a quarter of the decisions handed down concerned product families, with a family potentially including several dozen different products.

Moreover, the decisions issued provide a good illustration of the implementation of the Biocides Regulation, since the product types now subject to MA are widening: the decisions issued in 2019 concerned products with a variety of uses: household or professional disinfectants, insecticides, repellents, wood preservatives, preservatives for household products, preservatives for industrial fluids, etc.

Lastly, ANSES saw a high level of activity in the assessment of **biocidal active substances** this year. ANSES was almost the only organisation to send finalised assessment reports to ECHA for the EU review. In addition to the finalisation of these dossiers, the year saw the start of examination of two new active substances, along with the dossiers initially entrusted to the United Kingdom and transferred to France as a result of Brexit. This represented a total of eleven new dossiers in 2019.

ANSES's work in the area of biocidal active substances – Number of dossiers processed (2014-2019) as Rapporteur Member State and as a Member State involved in the European process

	2014	2015	2016	2017	2018	2019
Finalised assessment reports (first draft Competent Authority Reports – CARs) sent to ECHA	16	5	8	1	3	6
Assessment reports submitted by other Member States and commented on by ANSES	13	15	33	35	7	1*

**This very small number was due to the fact that in 2019, only one assessment report was submitted by the other Member States to ECHA. ANSES commented on this report.*

Phytopharmaco-vigilance

Phytopharmacovigilance, created under the French Act on the future of agriculture, food and forests in October 2014, is intended to monitor and detect any adverse effects on humans, farmed animals including honeybees, cultivated plants, biodiversity, wildlife, water and soil, air quality and food, following the use of plant protection products, as well as the emergence of resistance to these products. This scheme, which ANSES is responsible for implementing with the support of a network of partners designated by the regulations, enables information to be produced on a continual basis. Its output is used for risk assessment, placing products on the market and risk management missions by ANSES and the competent ministries and, more broadly, by all stakeholders involved or interested in the subject of risks associated with these products.

In 2019, ANSES continued to develop and ramp up this phytopharmacovigilance scheme (guided by its strategic orientation document for the period 2019-2021), with:

→ the investigation of reports of adverse effects,

→ the production and publication of summaries by active substance from the data available from the partner schemes,

→ the continuation or initiation of studies to consolidate the surveillance and data collection schemes that work in partnership with phytopharmacovigilance and generate new knowledge to meet phytopharmacovigilance objectives.

THE NETWORK OF PARTNERS IN PHYTOPHARMACOVIGILANCE

In 2019, the network of partners in phytopharmacovigilance was made up of schemes led by the Ministries of Agriculture, Health, Ecology and Consumer Affairs that provided monitoring data on foodstuffs, environmental water and drinking water, and of twelve other bodies: *Santé publique France*, the François Baclesse Centre, the Technical and Scientific Institute of Beekeeping and Pollination (ITSAP), the National Office for Hunting and Wildlife (ONCFS), the Central Laboratory for Air Quality Monitoring (LCSQA), approved air quality monitoring associations (AASQAs), the National Network for Monitoring and Prevention of Occupational Diseases (RNV3P), the Agricultural Mutual Insurance Scheme (MSA), poison control and monitoring centres (CAP-TVs), the "Toxinelle" scientific interest group, the Indoor Air Quality Observatory, and the "Soil" scientific interest group (GIS SOL).

COLLECTION AND INVESTIGATION OF REPORTS OF ADVERSE EFFECTS

In order for the phytopharmacovigilance scheme to be effective, appropriate tools are needed for identifying reports of adverse effects potentially related to plant protection products. Firstly, each year, ANSES's phytopharmacovigilance partners generate millions of data including reports of adverse effects or even alerts. In addition, declaration forms are provided on the ANSES website for professionals with a reporting obligation (MA holders, manufacturers, importers, distributors, professional users, advisers and trainers), but also for any other stakeholder including healthcare professionals and representatives from civil society. Lastly, literature monitoring also helps identify the results of scientific research that may be regarded as *real-life* reports of adverse effects.

The information collected is processed by ANSES in close collaboration with its partners and reporters, in order to classify the reports, the nature of the observed effects, their spatio-temporal magnitude, the circumstances under which they arose, their link with the incriminated plant protection products, and their potential impact on populations and their environment.

Several alerts and signals received by ANSES in 2019 led to in-depth analyses being initiated, in particular:

→ An alert by the association *Alerte des Médecins sur les Pesticides* (AMLP) on concentration levels in ambient air – qualified as high – reached occasionally by certain pesticides at a measurement site in the Bordeaux winegrowing area. This alert is being investigated within the broader framework of collective expert appraisal work on interpreting the results of the national exploratory campaign to measure pesticides in ambient air, funded by ANSES, implemented by the Central Laboratory for Air Quality Monitoring and the approved air quality monitoring associations, and whose results will be available in 2020.

→ Glyphosate in urine has been the subject of voluntary measurement campaigns by both citizens and farmers. The summary sheet of phytopharmacovigilance data on glyphosate was an opportunity to review the data available in the scientific literature on measurements of glyphosate in urine. The main results were published online in a "glyphosate" fact sheet in late 2019. It was found that the methods used varied greatly across studies, and rarely relied on rigorous sampling strategies. In addition, ANSES referred the matter to *Santé publique France*, its partner in the field of biomonitoring, mainly to compare the sensitivity and specificity parameters of the various existing analytical techniques. In 2021, additional data will be generated as part of *Santé publique France's* ESTEBAN programme (Health Study on the Environment, Biomonitoring, Physical Activity and Nutrition). Results for 900 adults and 500 children representative of the general French population, obtained using proven analytical techniques, will be available at the end of this study.

The other reports received in 2019 were investigated without, so far, any risk management measures needing to be recommended. Some have been included, together with other monitoring data, in the regular reviews prepared by ANSES or its partners, while others are currently undergoing more in-depth analyses.

SUMMARISED REVIEWS OF KNOWLEDGE FOR THE ASSESSMENT OF PLANT PROTECTION PRODUCTS

In order to make phytopharmacovigilance data available both to the ANSES teams responsible for assessing and re-assessing MAs and to any other interested parties, ANSES regularly reviews the available phytopharmacovigilance data on the active substances used in plant protection products. To this end, the Agency calls on its partners in order to obtain information from national monitoring and vigilance schemes.

The priority substances studied are those for which marketing authorisation applications or amendments are currently being examined by ANSES, some of which involve recently authorised substances. This information supplements the results of the *a priori* risk assessment from the dossiers submitted by applicants seeking MA renewal. Special attention is also paid to substances concerned by specific uses, or by agronomic, health or environmental issues in France, as well as to substances that are the subject of specific formal requests (expert appraisal on herbicide-tolerant varieties, expert appraisal on plant protection substances of concern). All the data collected for a substance or product in the framework of phytopharmacovigilance can also be reviewed to support the analysis of a report involving an adverse effect.

These reviews, in the form of fact sheets for each active substance, are regularly published on ANSES's website, along with an information note describing the sources and nature of the available information (https://www.anses.fr/en/content/phytopharmacovigilance-fact-sheets-more-information-plant-protection-substances). As an example, in 2019, fact sheets for glyphosate and copper were published.

ANSES regularly reviews the available phytopharmacovigilance data on the active substances used in plant protection products.

STUDIES TO CONSOLIDATE PARTNER SCHEMES, GENERATE NEW KNOWLEDGE, AND INVESTIGATE REPORTS

The information available through the phytopharmacovigilance scheme sometimes needs to be supplemented by strengthening the existing schemes or generating missing knowledge, for example, when a new warning signal emerges. ANSES undertakes specific studies for this purpose. These must be able to respond to precise questions with a view to rapid application to the MA conditions.

For the period 2018-2020, ANSES identified four strategic priorities for the studies:

→ Ambient air for the general population and for specific populations

→ Exposure and the impact on agricultural workers

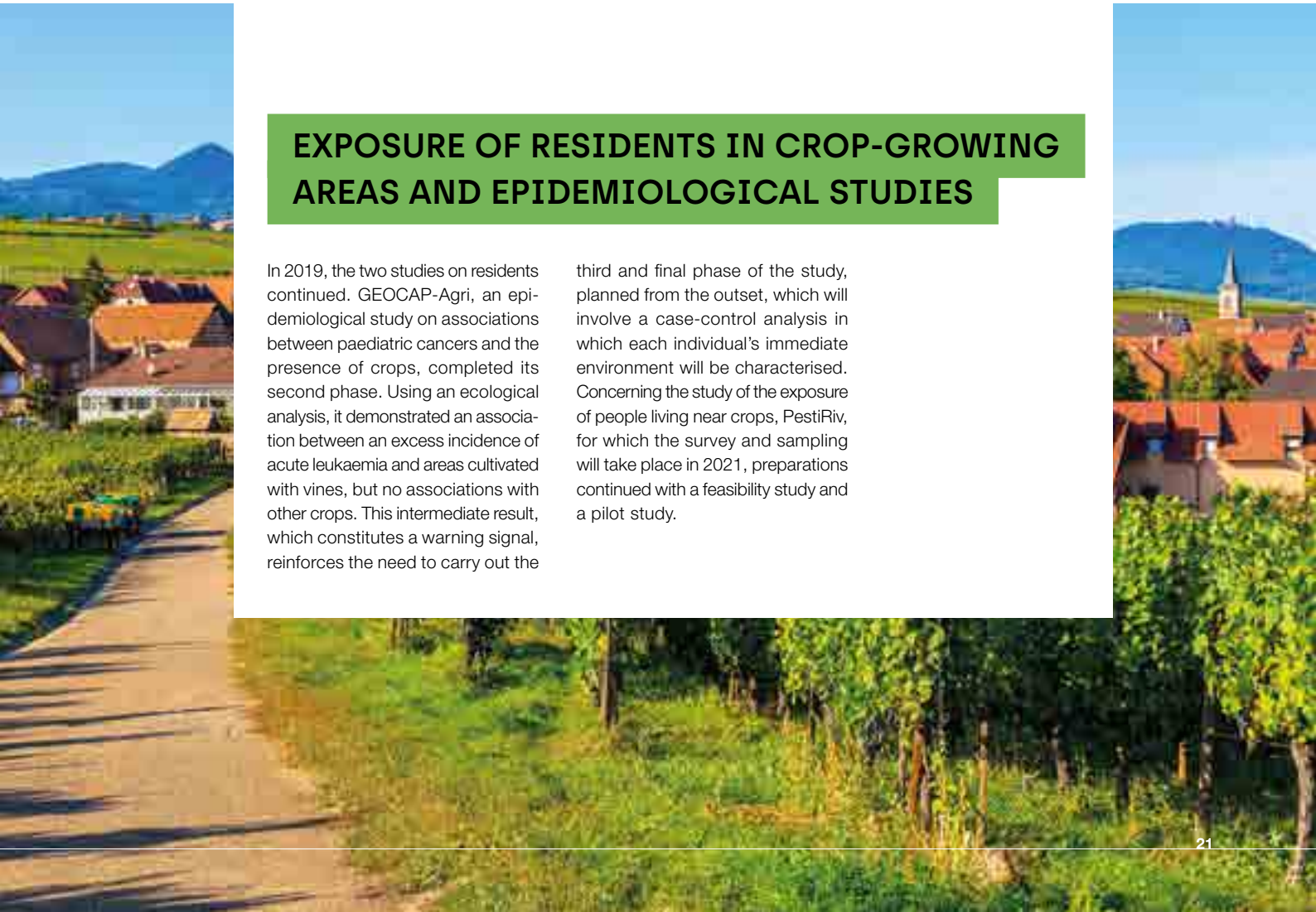
→ Bees and other pollinating insects

→ Biodiversity and environmental media (soil)

These priorities may be reviewed to take account of any changes in the phytopharmacovigilance scheme. ANSES can also undertake studies in emergency situations following alerts or new evidence requiring a signal to be investigated or more knowledge to be produced.

Since 2015, when the phytopharmacovigilance scheme was set up, 39 studies have been conducted:

	Studies under way in late 2019	Studies finalised in 2019
Animal health (including bees)	2	6
Human health (general population and workers)	11	10
Food	1	1
Biodiversity	1	2
Resistance	1	1
Environments (soil, water, air, etc.)	1	0
Other (data mining, etc.)	1	1
TOTAL	**18**	**21**



EXPOSURE OF RESIDENTS IN CROP-GROWING AREAS AND EPIDEMIOLOGICAL STUDIES

In 2019, the two studies on residents continued. GEOCAP-Agri, an epidemiological study on associations between paediatric cancers and the presence of crops, completed its second phase. Using an ecological analysis, it demonstrated an association between an excess incidence of acute leukaemia and areas cultivated with vines, but no associations with other crops. This intermediate result, which constitutes a warning signal, reinforces the need to carry out the third and final phase of the study, planned from the outset, which will involve a case-control analysis in which each individual's immediate environment will be characterised. Concerning the study of the exposure of people living near crops, PestiRiv, for which the survey and sampling will take place in 2021, preparations continued with a feasibility study and a pilot study.

EPIDEMIOLOGICAL STUDY ON SDHIS

Following initial expert assessment work carried out as a matter of urgency in 2019 in response to an alert issued by a team of scientists on the potential toxicity of succinate dehydrogenase inhibitor (SDHI) fungicides, ANSES concluded that the information available at the time and the hypotheses put forward did not provide any evidence to support a health alert, and also pointed out gaps in knowledge requiring the production of new data. This context led to the decision to fund a study to test the feasibility of retrospectively and prospectively monitoring changes in the incidence of known diseases involving "SDH" mutations: PGL. EXPO. Its main objective will be to test the hypothesis that SDHI exposure may contribute to the emergence of tumours in patients (paragangliomas, pheochromocytomas and, more rarely, kidney cancers and gastrointestinal stromal tumours). At the time of publication of this report, ANSES was nevertheless informed by the study sponsors that its launch has been postponed, given their mobilisation in combating the COVID-19 epidemic.

STUDY OF PESTICIDE RESIDUES IN SOIL

In 2018, ANSES funded a three-year prospective study on the measurement of pesticide residues in soil, with the help of the French institutional soil monitoring network: the Soil Quality Measurement Network (RMQS), led by the "Soil" scientific interest group (GIS SOL). Sampling began in 2019 and will continue in 2020, depending on the constraints of the epidemic situation. The results of this study are eagerly awaited, as they will make it possible to assess the feasibility and relevance of using the RMQS to set up a regular monitoring scheme for pesticide residues in soil, on a national scale.

PESTI'HOME A STUDY ON THE USE OF PESTICIDES IN THE HOME

Within the framework of the Pesticide Residues Observatory and in conjunction with the phytopharmacovigilance scheme, the results of the metropolitan part of the *Pesti'home* study were published in 2019. They show that pesticide use in the home concerns three-quarters of households and predominantly involves insecticides, which are used both as biocides and to protect pets and plants. Domestic users of pesticides are relatively uninformed about the products' conditions of use and authorisation status, which therefore need to be better communicated.

The Agency's other activities in the area of regulated products

Besides assessment and placing on the market of plant protection and biocidal products, ANSES carries out specific studies, whether in response to formal requests, on its own initiative or as part of European projects, with input from many other ANSES activities.

Many hazard and risk assessment studies are also conducted. These contribute to the decisions made on issuing authorisations, including:

→ an opinion on the assessment of a warning signal regarding the toxicity of succinate dehydrogenase inhibitor (SDHI) fungicides (see below),

→ two opinions, the first on provisions for reducing the exposure of bees and other pollinating insects to plant protection products, and the second recommending further development of risk assessment methods in the context of marketing authorisation applications (see box),

→ an opinion on the endocrine-disrupting properties of epoxiconazole,

→ an opinion on the assessment of urease and nitrification inhibitors with regard to risks to the environment and human health,

→ two opinions on risk assessment and the protection of residents and bystanders during the use of plant protection products (see box),

→ a proposed study plan to improve knowledge on the carcinogenic potential of glyphosate (see box below),

→ an opinion on substances identified as being of concern in plant protection products[5].

ANSES's opinions are published on the Agency's website accompanied by news updates.

In 2019, ANSES also initiated various studies, including an assessment of the warning signal concerning the toxicity of succinate dehydrogenase inhibitor (SDHI) fungicides and on the subject of antimicrobial resistance.

In early 2019, after being alerted by a group of scientists, ANSES published an opinion on the assessment of a warning signal regarding the toxicity of SDHI fungicides. Based on a review of all the scientific data available up to 2018, carried out by a group of independent experts, ANSES concluded that there was no health alert justifying the withdrawal of marketing authorisations for these fungicides. However, it called for vigilance at European and international level and stressed the need to step up research on potential toxicological effects in humans. During 2019, ANSES therefore continued its work on the potential health effects of these substances based on three lines of investigation:

→ Advancing knowledge through the definition and funding of specific research projects and the start of work on the issue of cumulative exposure to different SDHIs via food,

→ Detection of possible health effects that can be observed in the field via existing monitoring schemes (see Section 8),

→ Interaction with research bodies and health agencies responsible for assessing these substances, in particular EFSA.

In 2019, ANSES carried out a comparative assessment of glyphosate-based products with non-chemical alternatives commonly used in France, in application of Article 50.2 of Regulation (EC) No 1107/2009 and following a ministerial instruction. This comparative assessment was implemented as part of a review of applications to renew the authorisations for these products. This work was carried out mainly on the basis of INRAE reports for uses in viticulture, arboriculture and field crops. It began in 2019 but will continue throughout 2020.

Lastly, ANSES provided scientific and technical support to the Ministries concerned on the draft regulation establishing rules for the placing on the market of fertilisers bearing the CE mark and amending Regulations (EC) No 1069/2009 and (EC) No 1107/2009, which has now been adopted.

[5] This opinion was signed in late 2019 but published in the first half of 2020.

BEES

→ To reduce the exposure of bees and other pollinating insects to plant protection products, in its Opinion of 23 November 2018, ANSES recommended strengthening the national provisions imposing restrictions on use of these products during periods when crops are attractive to these insects. The Agency also published a new opinion aimed at improving risk assessment methods in the context of marketing authorisation applications. ANSES recommends relying on the EFSA guidance document, in order to better assess the long-term risks for bees and other pollinators. In addition, the Agency stresses the need to set regulatory threshold values for chronic risks at European level, in order to harmonise the criteria used for making decisions on product marketing authorisations.

GLYPHOSATE SPECIFICATIONS

→ **Glyphosate is an active substance used in many herbicidal products, whose approval was renewed for five years by the European Union in December 2017. Following the controversies over the carcinogenic classification of glyphosate, ANSES issued a call for tenders for several toxicological studies to improve knowledge of the carcinogenic potential of this substance.**

PROTECTING THE HEALTH OF RESIDENTS

→ Protecting populations when plant protection products are used is a regulatory requirement. For each marketing authorisation application, ANSES therefore assesses the health risks to operators and workers, but also to bystanders and residents, and specifies minimum distances to be complied with during treatment. Pending a re-assessment of the products and changes to existing marketing authorisations in June 2019, ANSES recommended establishing minimum safety distances at values at least equal to the distances taken into account in the assessments, as well as the widespread use of devices to limit drift. As a precautionary measure, it also recommended increasing these distances for products containing active substances with assumed or suspected carcinogenic, mutagenic or reprotoxic effects. In December 2019, ANSES published an additional opinion on the different ways of reducing exposure to product drift during spraying.

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French agency for food, environmental and occupational health & safety

Investigate, evaluate, protect

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