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Post-MA surveillance of veterinary medicinal products

2021 annual report

October 2022

INVESTIGATE, EVALUATE, PROTECT

Post-MA surveillance of veterinary medicinal products

2021 Annual Report

French Agency for Veterinary Medicinal Products (ANMV)

October 2022

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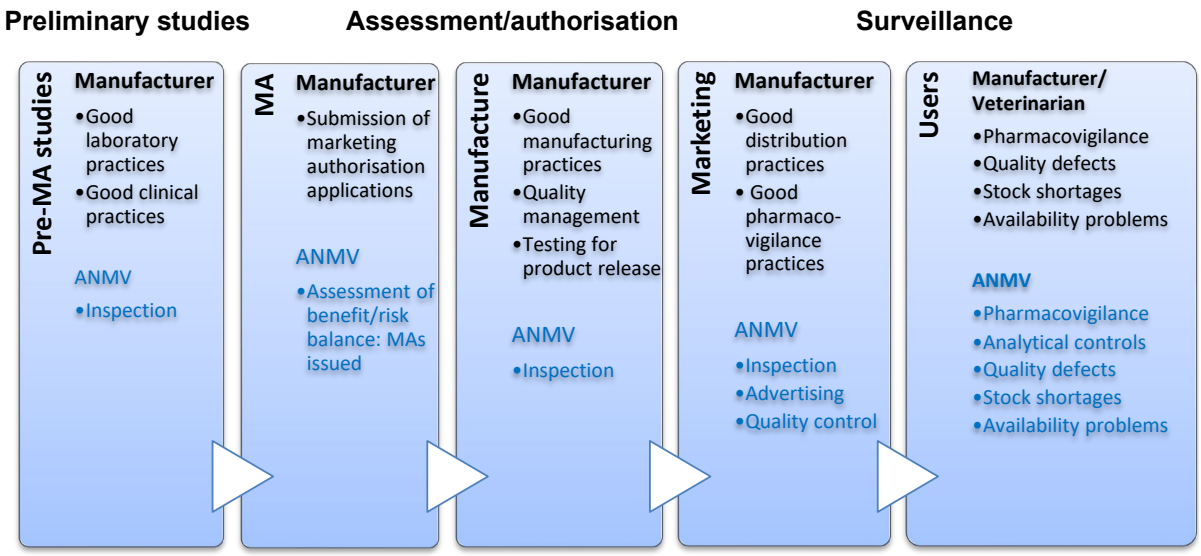
A/ ANSES and post-MA surveillance of veterinary medicinal products

Veterinary medicinal products are mainly governed by European regulations. ANSES, through the French Agency for Veterinary Medicinal Products (ANMV), is the competent authority for assessing and managing risks associated with veterinary medicinal products in France. Its missions are carried out as part of a European network led by the EMA (European Medicines Agency).

The ANMV, part of ANSES, is responsible for ensuring that prescribers and animal owners are provided with veterinary medicinal products that are safe, effective and of good quality. In order to fulfil this task, the Agency intervenes in all stages of the veterinary medicinal product lifecycle:

- **It assesses** national or European marketing authorisation applications for veterinary medicinal products and takes part in the assessment of European dossiers on maximum residue limits (MRLs) of veterinary medicinal products in foods of animal origin. Prior to assessing applications, it can intervene as early as the medicine testing phase by inspecting the laboratories implementing the trials.
- **It grants** marketing authorisations for medicinal products, and authorises clinical trials of these products and the opening of pharmaceutical establishments (licensed operators known in France as *exploitants*, wholesalers, manufacturers, exporters and/or importers of veterinary medicinal products). It certifies imports and exports of veterinary medicinal products.
- Once a medicine has been brought to market, **the Agency monitors** the occurrence of any adverse effects resulting from its use, as well as problems of availability on the French market. It controls quality through testing, assessing reports of quality defects and verifying advertising materials on veterinary medicinal products. The Agency also monitors the operation of pharmaceutical establishments and other industrial veterinary facilities.



Once the veterinary medicinal products have been granted authorisation, surveillance involves:

- **Inspecting pharmaceutical establishments** and other veterinary facilities falling within the scope of ANSES-ANMV inspections, to ensure the quality, safety and efficacy of medicines developed, manufactured and distributed in France (Chapter B);
- **Market surveillance**, which includes monitoring veterinary medicinal product quality through expert appraisals and management of quality defects, analytical control of veterinary medicines, verification of labelling and advertising, as well as monitoring stock shortages (Chapter C);
- **Monitoring adverse effects** through veterinary pharmacovigilance (Chapter D).

This report covers all the results related to the surveillance of veterinary medicinal products marketed in France for 2021.

B/ Inspection activities

As of 31 December 2021, an authorisation had been issued for one or more activities (manufacture, wholesale distribution, *exploitation*, etc.) to **321 veterinary pharmaceutical establishments**.
In addition to these authorised establishments, ANSES-ANMV also inspects other facilities involved in the development or manufacture of veterinary medicinal products (test facilities and sites, radiosterilisation facilities, quality control laboratories), as well as test facilities that carry out safety trials.

These figures are stable compared with previous years.

Breakdown of veterinary pharmaceutical establishments authorised in France and other industrial facilities inspected in 2021, according to their main activity.

To ensure access to safe, effective and good quality veterinary medicinal products, the ANSES-ANMV surveillance scheme relies heavily on inspections of pharmaceutical establishments and other veterinary facilities.

These regular inspections, based on a risk analysis, ensure that pharmaceutical and other veterinary facilities implement quality practices in accordance with the applicable regulations and best practices, and enable these facilities to maintain their certifications throughout the medicinal product lifecycle.

The annual inspection plan is based on a risk analysis that takes into account regulatory requirements, the results of previous inspections (compliance history), the intrinsic risk associated with the activities carried out by the pharmaceutical establishment or veterinary facility, any reports received, requests from internal or external sponsors, and any campaigns on a particular topic. It also takes into account the available inspection resources at the ANMV (6 inspectors in 2021).

This plan defines a "List 1" of priority establishments, as well as a "List 2" of lower priority establishments.

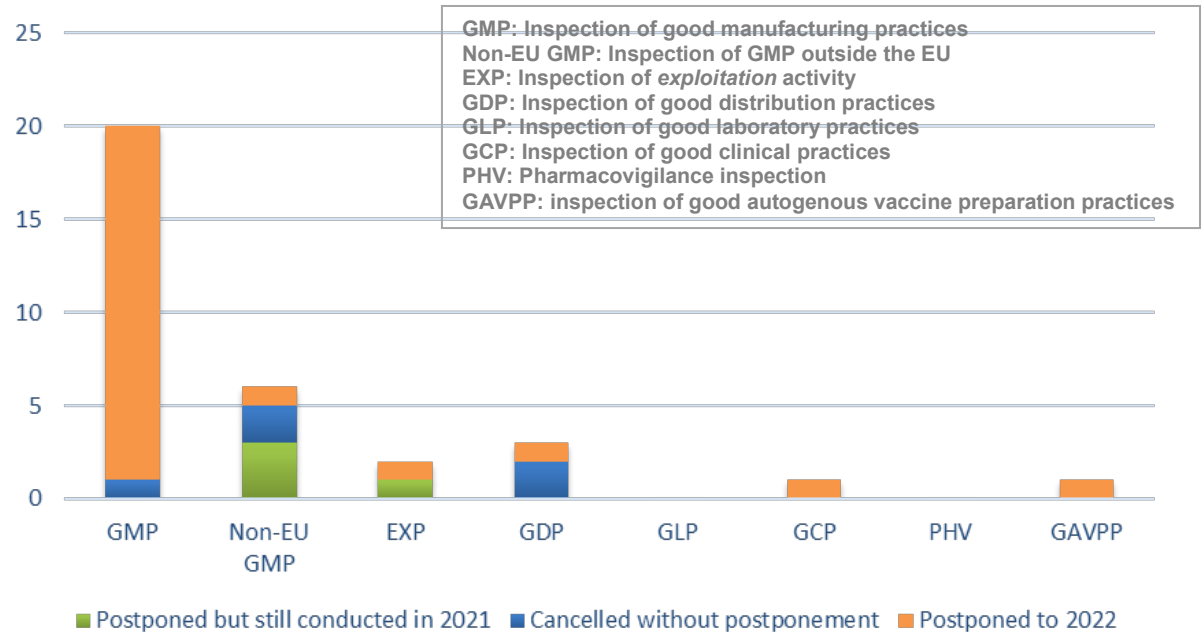
Because of the health context due to the COVID-19 epidemic, travel was either limited (nationally) or ceased completely (internationally) during this period.

As a result, 33 missions were affected by an event that prevented them from being carried out on the dates initially set in 2021:

- Twenty-one missions were affected directly or indirectly by the health crisis (COVID organisation, planned workload, training of key personnel, mandatory meetings, etc.), mainly by the travel restrictions:
    - two missions concerning French sites were able to be rescheduled later in the year;
    - one mission concerning a site in a third country was cancelled due to a cessation of activity;
    - eighteen missions concerning sites in third countries were postponed to 2022 without any health impact, due to the European decision to automatically extend the validity of GMP certificates until 31/12/2022.

- Twelve other missions were impacted by other events (delays in launching operations, cessations of activity, etc.):
    - seven missions were rescheduled to 2022;
    - five were cancelled due to site closures or cessation of a site's activity in the veterinary field.

Inspections postponed in 2021, by field



In the end, 66% of the establishments on List 1 (48 out of 73) were inspected; the unfulfilled inspection missions were due to cessations of activity or postponements of the inspection to 2022 due to the general context. This then enabled 17 inspection missions on List 2 to take place.

The inspection unit continued to use the new inspection approach (remote inspection) developed in 2020 to adapt to the emerging constraints. In 2021, 13 inspection missions took place according to this new configuration.
In addition, the annual inspection plan generally includes unannounced visits. In 2021, by decision of the ANMV management and in line with government measures, no unannounced visits were carried out.

Lastly, seven missions were carried out to meet unexpected requests for urgent health inspections or investigations.

Four GMP inspections of establishments located in third countries were carried out, including three at the request of the EMA (European Medicines Agency). All these inspections were carried out remotely.

Key inspection figures from 2021

(GMP: Good manufacturing practices, GDP: Good distribution practices, GLP: Good laboratory practices, GCP: Good clinical practices, GAVPP: Good autonomous vaccine preparation practices, PhV: pharmacovigilance, EXP: *exploitant*)

The 2021 review of inspections shows:

- Just as in 2020, the deviations among manufacturers of veterinary medicinal products mainly concerned validation (of processes, cleaning and equipment), the quality system (management of deviations and preventive and corrective measures), production (environmental monitoring, documentation and production control) and quality control (sampling, microbiological testing, etc.).
- For *exploitants* and wholesalers, the points requiring attention related to schemes for monitoring and improving quality (mainly regarding cold chain management, handling and following up non-compliances and complaints, and quality risk management).

Two inspections of the pharmacovigilance scheme took place at the request of the EMA in 2021. They were carried out remotely. The pharmacovigilance schemes are also supervised through inspections of the *exploitation* activity. The results show deviations in the exercise of responsibility by the person in charge of pharmacovigilance (QPPV), in the management of adverse effect reports and in training.

As part of veterinary medicine research and development, 30 establishments are registered in the "Testing facility" programme. Thirteen GLP inspections, included in the annual inspection plan, were carried out in 2021. They are designed to verify that good practices are followed when carrying out laboratory tests for non-clinical trials, for the purpose of marketing authorisation applications. These primarily serve to guarantee the safety of the veterinary medicinal products tested.

Some inspections were initiated in 2021 as part of the project on good clinical practice (GCP) and assessing the compliance of clinical studies carried out in France. The pilot phase is expected to end in 2022.

No formal notice was served to any of the establishments or facilities visited by ANSES-ANMV inspectors in 2021.

The 2021 inspection plan ensured overall compliance with regulatory inspection frequencies and maintained the validity of certifications issued for veterinary pharmaceutical establishments. In 2021, 72 establishments of all categories were inspected, compared with 59 in 2020.

C/ Market surveillance

Market surveillance includes monitoring veterinary medicinal product quality through expert appraisals and management of quality defects, analytical control of veterinary medicines, and verification of labelling and advertising. This activity also includes determining the legal classification of products and monitoring stock shortages.

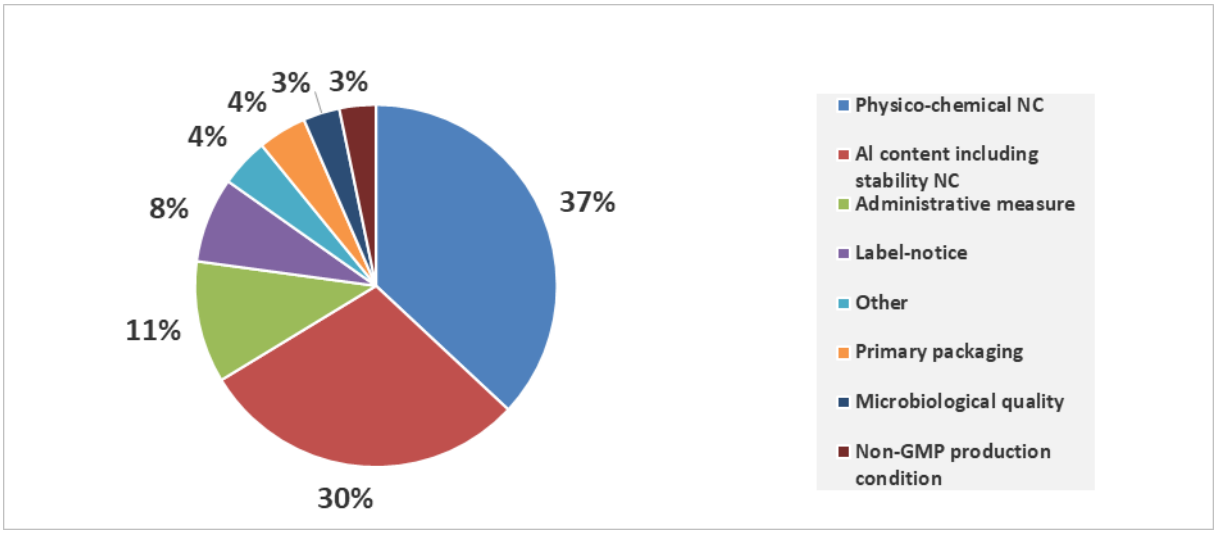
C1 – Quality defects

In 2021, 91 reports of quality defects were recorded. This number is in line with the average results observed over the last ten years, following a slight decrease in 2020 (with 81 reports).

The majority of reports still came from companies. However, three quality defects were reported by professionals (two by veterinarians and the third by a pharmacist) and four others by the ANSES-ANMV analysis laboratory as part of its annual control plan for medicinal products on the market.

As in previous years, most quality defects concerned non-compliance with the specifications on active ingredient content or other physico-chemical specifications. These non-compliances were mostly discovered during the monitoring of stability studies of medicines. The breakdown is shown in the figure below:

Breakdown of quality defects monitored in 2021



(NC = non-compliance; GMP = good manufacturing practices)

Each quality defect undergoes a risk analysis that takes into account the severity of the harm caused, the probability of its occurrence and all the factors specific to the case in question: whether or not harm has actually been observed in the field, marketing of the products, detectability of the defect, etc. The resulting score is used to classify the risk level, which determines the appropriate level of recall – ranging from no recall through to the public being informed.

Batch recalls involve the withdrawal of a batch of non-compliant veterinary medicinal products already on the market. This withdrawal may be limited, i.e. it may concern only certain stages of the distribution circuit (e.g. wholesale distribution), only certain distributors or users, or only certain specific batches.

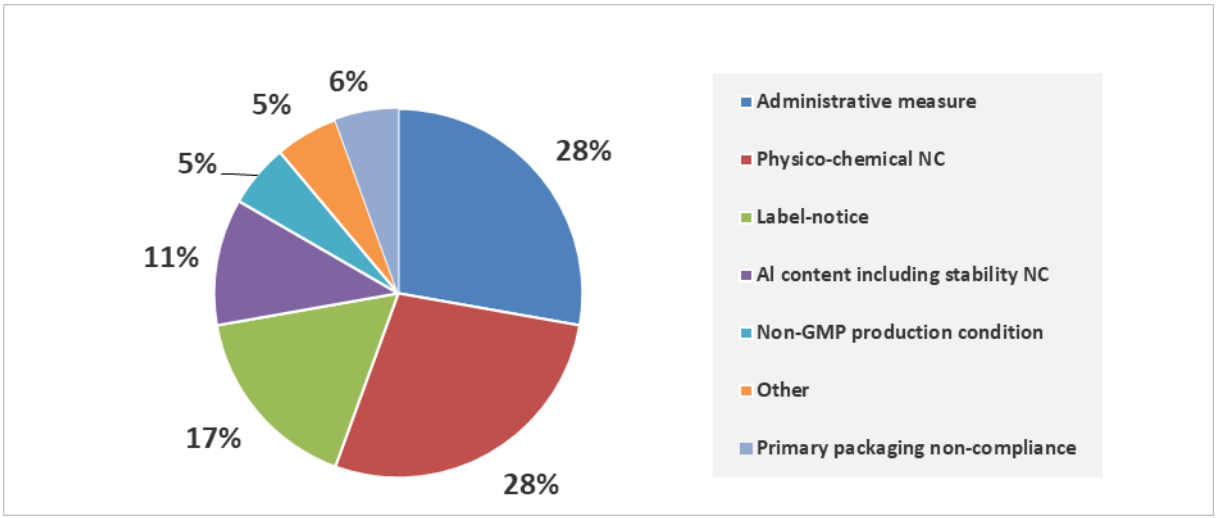
The quality defects reported in 2021 were mostly assessed as posing minor risks, and therefore in 77% of cases did not lead to a batch recall.

In the other cases (18 reports), batch withdrawals were mostly limited to the manufacturer or depository level (12), or to wholesale distributors (4).

Only two recalls involved retailers, prescribing veterinarians or pharmacists, which represents about 2% of the cases and 10% of the recalls. This trend is similar to other years.

Two-thirds of batch recalls were the result of either administrative measures (changes in withdrawal times, expiry dates, dispensing conditions, etc.) or non-compliance with physico-chemical specifications.

Breakdown of reasons for batch recalls in 2021



(AI = active ingredient; NC = non-compliance; GMP = good manufacturing practices)

C2 – Analytical quality control of veterinary medicinal products

Selected veterinary medicinal products are subject to analytical control according to an annual programme. It is drawn up on the basis of a risk analysis and in such a way that it is representative of all therapeutic categories and dosage forms, and also covers the vast majority of veterinary sectors.

This list of veterinary medicinal products is then supplemented by requests from other ANSES-ANMV departments (scientific assessment, pharmacovigilance, quality defects monitoring, non-compliance monitoring) or from the field. In addition, a rating grid for medicinal products is now available in Europe for classifying these products in terms of their risk levels. The veterinary medicinal products rated and identified as posing the greatest risk are included in the annual control programme.

In 2021, 145 medicinal products were analysed with 544 tests carried out mainly by the ANSES-ANMV laboratory. Some tests that could not be performed by the ANSES-ANMV laboratory were carried out by other laboratories in the European Network of Official Medicines Control Laboratories (OMCL Network).

Seven medicines were found not to comply with the MA specifications, i.e. a non-compliance rate of 4.8% (compared with 13% in 2020).

The non-compliances identified concerned the following:

- pH (1),
- breakability (1),
- active substance content (2),
- labelling (3).

Four of these non-conformities were monitored as quality defects and have now been closed. The other three concerned labelling changes that have been included in the 2022 control plan.

As well as carrying out the annual control programme, the laboratory was consulted in connection with a legal requisition for the analysis of seized Spanish medicines.

C3 – Advertising control

Advertising of veterinary medicinal products is regulated by Regulation (EU) 2019/6 and by the French Public Health Code (CSP). It only covers authorised veterinary medicinal products. Advertising to the public is only permitted for non-prescription medicinal products. Depending on the type of medicinal product and/or the recipient, advertising materials are subject to either prior declaration or authorisation. For more information, a guide to good advertising practices is available on the ANSES website[1].

Advertisements requiring prior authorisation concern antimicrobials, medicinal products subject to a risk management plan, medicinal products indicated for Category 1 health hazards, medicinal products containing anabolic, anticatabolic or β-agonist substances, and lastly advertisements for all medicines intended for the general public.

In 2021, 690 advertising applications led to 1718 advertising materials being checked, which was a 20% increase in the number of applications and a 28% increase in the number of advertising materials compared to 2020.

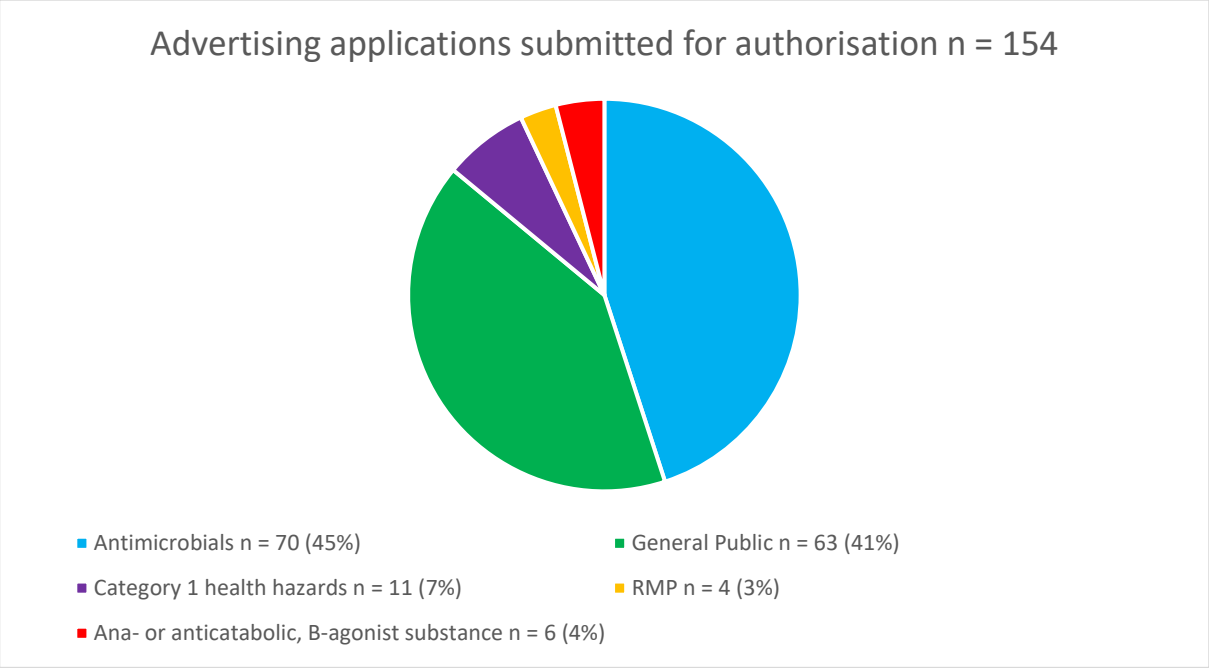
Of the 690 applications submitted, 154 concerned advertising requiring authorisation, and 536 advertising subject to simple declaration. This breakdown was comparable with the data from previous years, with applications requiring authorisation accounting for between 20 and 25% of the total.

No refusals of publication were notified in 2021.

The vast majority of applications requiring authorisation concerned medicinal products intended for the general public (non-prescription medicines). Among prescription medicines, the submissions mainly concerned antimicrobials.

1 https://www.anses.fr/fr/system/files/20220808_Guide%20des%20BPP_Anmv_version%20n%C2%B06_v1_ANMV_version%20finale.pdf

Breakdown of advertising applications submitted for authorisation in 2021



(RMP = Risk Management Plan)

C4 – Classification of "borderline" products

When notified of such cases, ANSES-ANMV carries out work to classify so-called "borderline" products. Based on the presentations and claims made, this process seeks to determine whether or not the products in question can be defined as veterinary medicines.

In many cases, this concerns products on the boundary with biocides or animal feed. This activity has been structured within the Market Surveillance and Pharmacovigilance Unit, and mainly involves use of a generic assessment grid.

In 2021, ANSES-ANMV received 78 requests concerning around 300 products. This was a 30% increase compared with 2020, but reflected a return to the normal average from before the health crisis.

Of these requests, 21 cases were on the boundary with feed products, 27 with medical devices and seven with biocidal products. These reports or requests for regulatory opinions came from authorities, companies, health professionals and individuals.

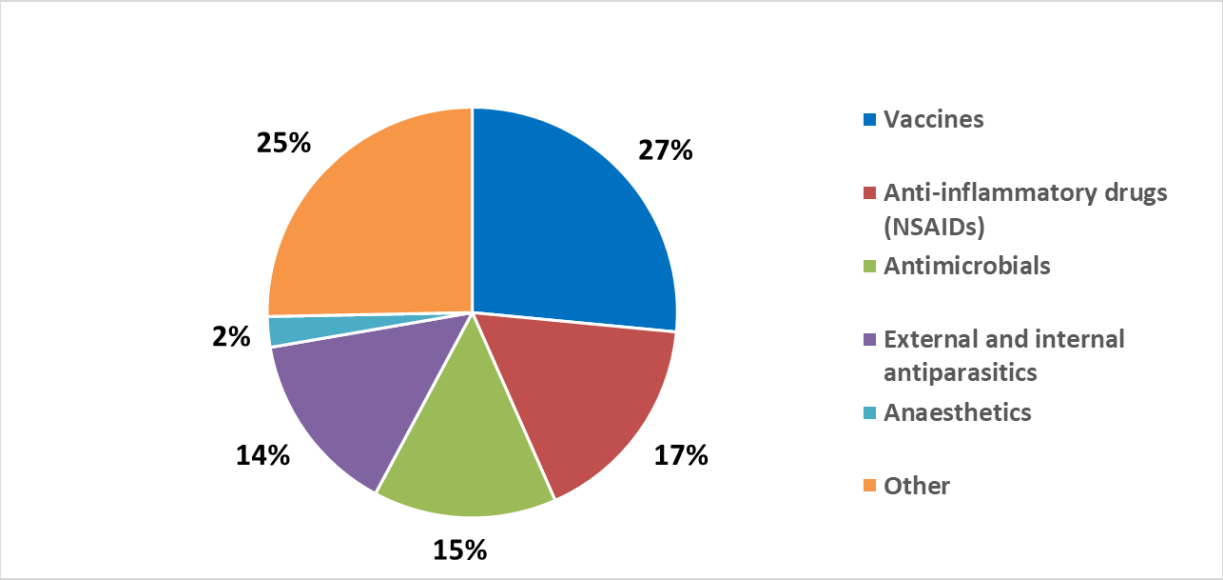
Twenty-three cases concerned one or more products that were then classified as veterinary medicinal products. In the vast majority of cases, the manufacturer rectified their status following a request from the ANMV to bring the products into compliance. One company failed to make any corrections, and was served formal notice for its StopVarroa website, which offered a so-called miracle product against varroasis in bees. This product, although falling under the definition of a veterinary medicinal product, was sold without marketing authorisation and therefore without having been assessed in Europe for its quality, safety and efficacy. The company illegally marketing this unauthorised medicine was located in a third country, illustrating the difficulties faced by the authorities in regulating internet sales.

C5 – Management of shortages of veterinary medicinal products

The companies marketing the medicinal products report any stock shortages to ANSES-ANMV. These reports are used to identify proven stock shortages and their impact on practitioners and animal owners as early as possible, in order for possible alternatives to be identified and information on critical stock shortages to be published.

In 2021, 83 shortages were reported, a figure equivalent to that of 2020.

Breakdown of stock shortages by type of medicine in 2021



Vaccines were the main category of medicines affected by shortages in 2021 (27%), with a significant number reported for vaccines for dogs and cats. These shortages are the consequence of the strong market growth (+20%) due to the increase in the number of dogs and cats in French households.

The other three main categories of medicines (antimicrobials, steroidal and non-steroidal anti-inflammatory drugs, and internal and external antiparasitics) each accounted for about 15% of shortages.

A stock shortage is said to be critical when it could introduce a risk to human health, animal health and welfare. The criticality analysis takes into account various criteria: impact of the shortage on human and animal health, other medicines available for the disease in question and their respective market shares, estimated duration of the shortage, economic impact of the shortage on the sector in question (avian, equine, etc.).

In 2021, six new critical stock shortages were published on the ANSES website. Alternative solutions were found each time. This online information is regularly reviewed to provide clarification or updates on when products again become available on the market, or to inform practitioners about alternative solutions identified over time. Seven critical shortages were also closed.

In particular, ANSES-ANMV took action to ensure the **availability of vaccines against equine rhinopneumonitis caused by equine herpes virus (EHV1)**, following the spread of an EHV1 rhinopneumonitis outbreak in horses in various European countries. This outbreak led to a sharp increase in sales of the two vaccines authorised on the French market (Equip® EHV 1,4 produced by Zoetis, and Pneumequine® by Boehringer Ingelheim) from early March.

As MA holders are required to inform ANSES of any risk of a critical shortage, the Agency was promptly informed of the upcoming "critical" situation by the two pharmaceutical companies concerned. ANSES-ANMV was thus able to work with them both, facilitating the exchange of information on all the batches that were potentially available or could be made available in the short term. It also quickly gave exceptional approval to extend the expiry date for two batches of vaccines. This avoided a total breakdown in vaccine supply, which could have lasted several weeks and would have been very detrimental to the equine sector as a whole.

These actions are in line with the good practices for managing shortages in veterinary medicinal product supplies, updated in 2021[2].

[2] https://www.anses.fr/fr/system/files/BP%20ruptures%20approvisionnement%20juin%202021.pdf

D/ Pharmacovigilance

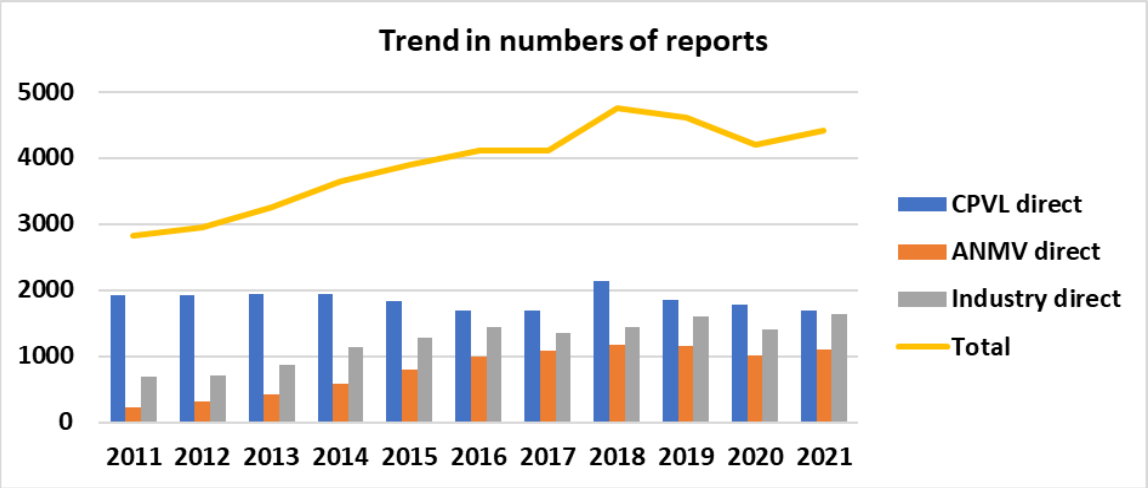
D1 – 2021 review

- Trend in total numbers of reports of adverse events

In 2021, 4420 pharmacovigilance reports were notified to ANSES-ANMV, representing a 5% increase in the total number of reports compared to 2020.

These data correspond to the number of reports of adverse events occurring in animals or humans following administration of/contact with a veterinary medicinal product or, in the framework of the "cascade" approach, adverse effects occurring in animals following administration of a medicinal product designed for human use.

Trend in numbers of reports from 2011 to 2021 according to reporting channels



ANMV direct: reported via the online submission site; CPVL direct: animal cases reported to the CPVL by post/email or telephone, as well as human cases recorded by poison control centres; Industry direct: reported to the MA holder.

Of the 4420 reports received, 4093 concerned animals and 327 related to humans. The majority of reports relating to humans came from poison control centres (85%). As for the cases concerning animals transmitted directly to the ANMV and the CPVL, veterinarians remained the main sources of reports (90%).

The typology of the reports remains globally similar to that observed in previous years, with the vast majority concerning adverse effects in animals (78% of the total number). The number of reports of suspected lack of efficacy remained below 15% (13% in 2020 as opposed to 15% in 2019 and 8-10% in previous years).

In animals, the total number of reports increased again in 2021, following two years of decline. The proportion of serious/non-serious reports remained the same as in previous years: 60% serious and 40% non-serious.

Typology of reports in 2021

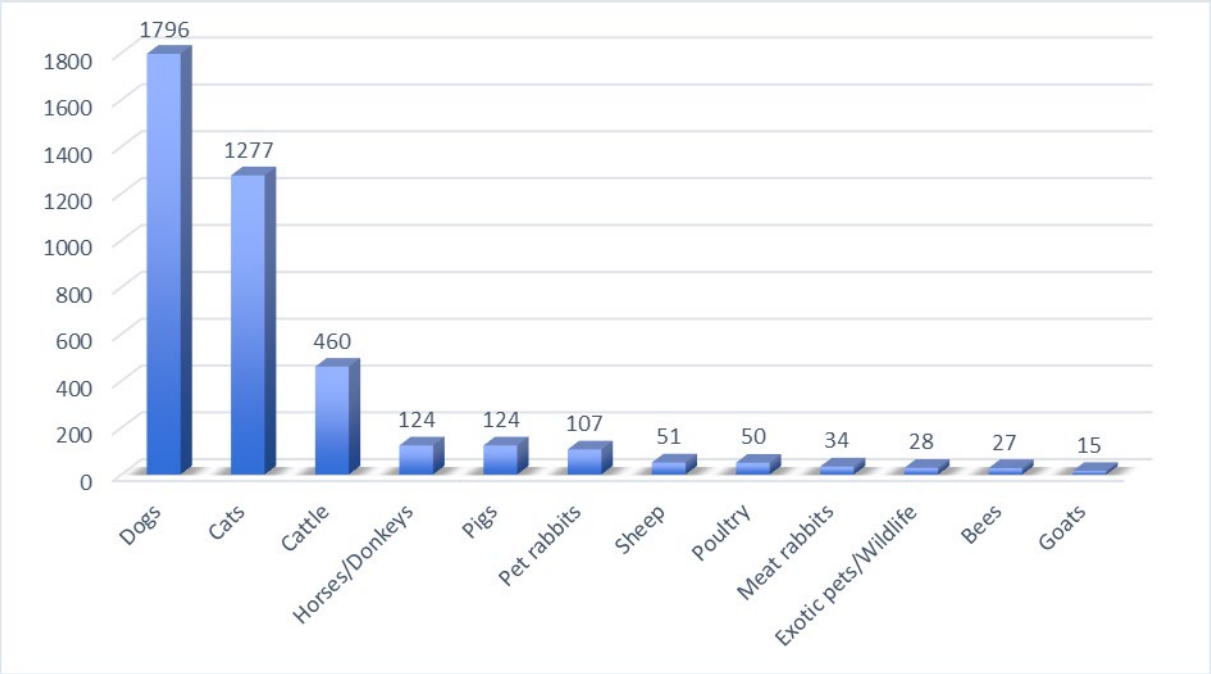
Typology of reports	Number	%
Adverse effects in animals	3435	77.71
Lack of efficacy	643	14.55
Residue issues	14	0.32
Environmental issues	0	0.00
Transmission of infectious agents	1	0.02
Adverse effects in humans	327	7.40
Total	**4420**	**100.00**

One report related to a suspected transmission of infectious agents was recorded in 2021. This case was described in the scientific literature: ECLERCY. J et al. Phenotypic and Genetic Evolutions of a Porcine Reproductive and Respiratory Syndrome Modified Live Vaccine after Limited Passages in Pigs. Vaccines 2021, 9,392. The report was deemed inconclusive due to a lack of confirmation of reversion to virulence, despite virus typing.

- Reports by species and therapeutic category

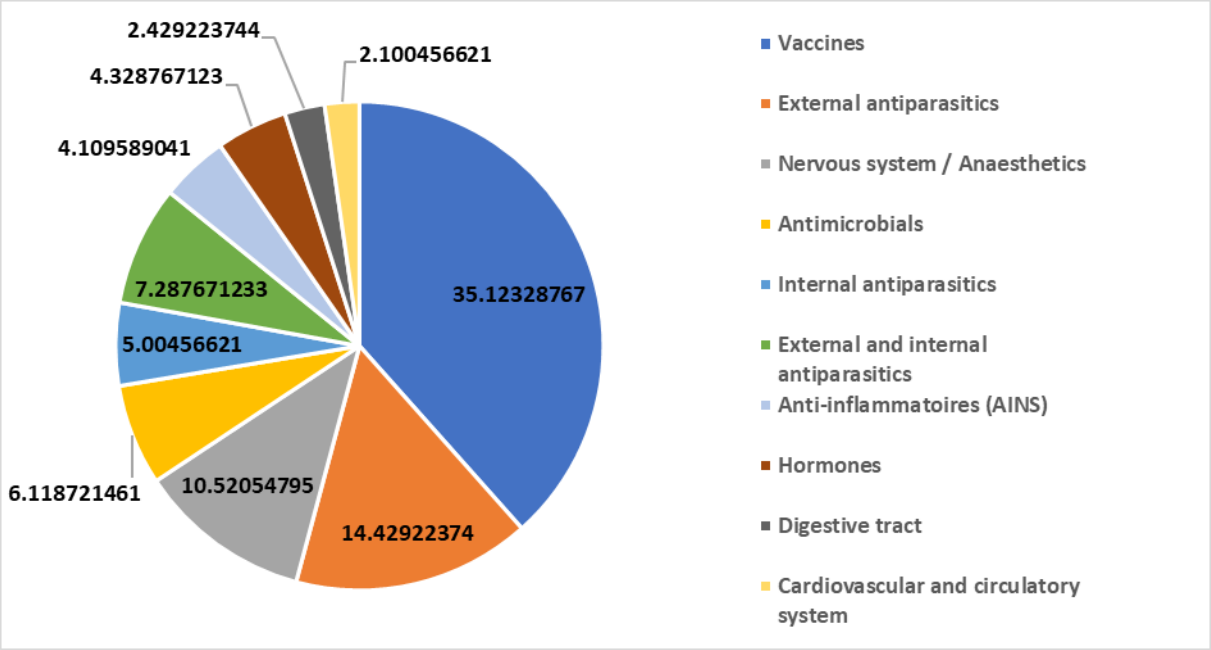
Since a single report may concern several medicinal products, a total of 5475 medicines were involved in the 4420 reports. As in previous years, domestic carnivores again accounted for more than 80% of reports involving animals.

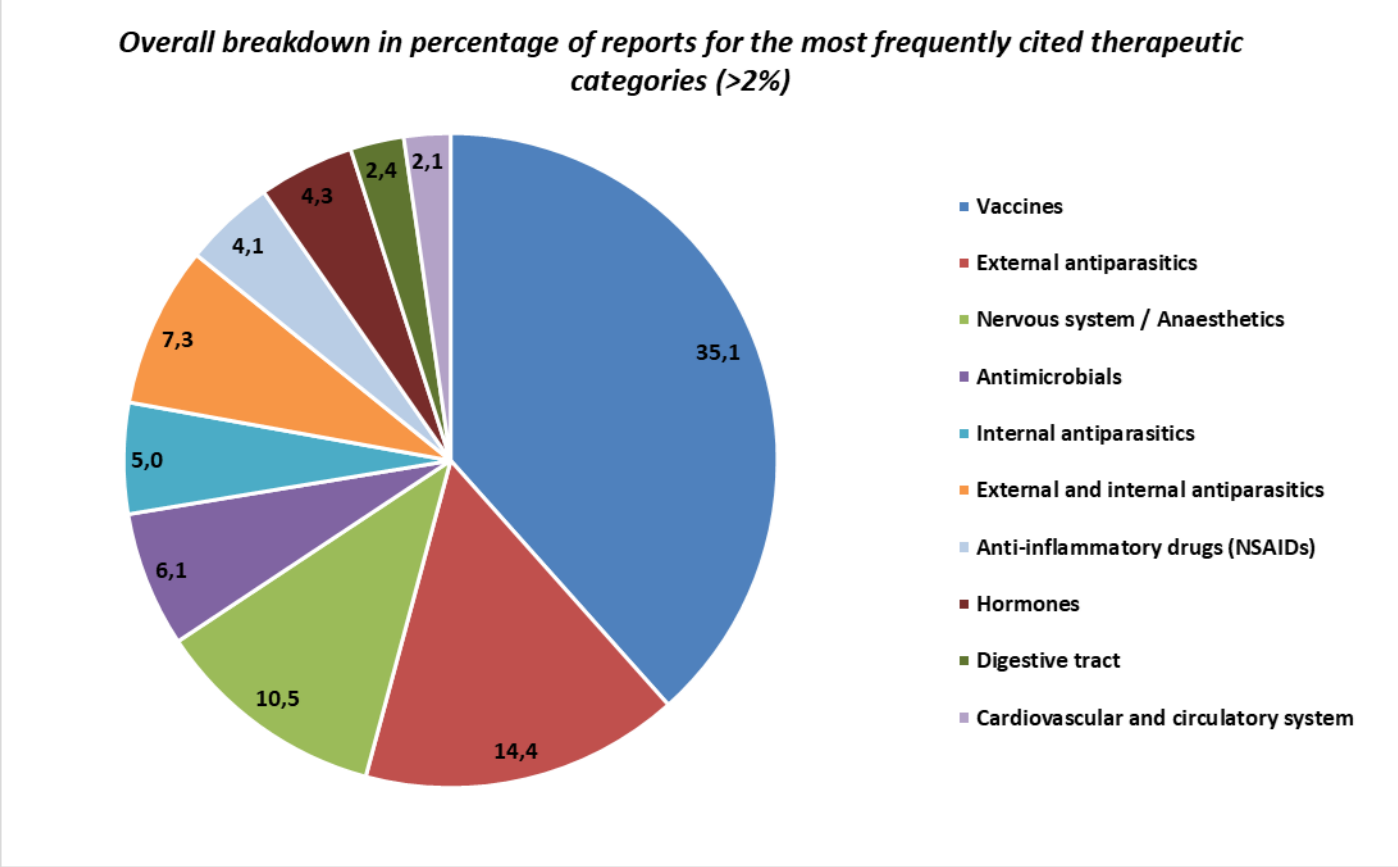
Breakdown by affected species in 2021



Vaccines remained the main products incriminated in an adverse event in most species. However, in bees, external antiparasitics were the most frequently cited, and in exotic pets/wildlife the predominant therapeutic category was endectocides.

Overall breakdown in percentage of reports for the most frequently cited therapeutic categories (>2%)





Breakdown by therapeutic category of the number of reports according to species in 2021

	Dogs	Cats	Cattle	Horses/ Donkeys	Pigs	Pet rabbits	Sheep	Bees	Poultry	Goats	Exotic pets/	Meat rabbits	General total
Vaccines	797	347	360	53	163	76	26	0	51	6	5	39	1923
External antiparasitics	420	311	6	2	1	16	0	30	0	2	2	0	790
Nervous system/Anaesthetics	288	231	10	32	1	8	4	0	1	1	0	0	576
Antimicrobials	92	66	130	27	5	7	2	0	1	2	3	0	335
Internal antiparasitics	111	78	30	18	7	0	15	0	5	2	8	0	274
External and internal antiparasitics	94	242	25	8	0	4	19	0	0	2	5	0	399
Anti-inflammatory drugs (NSAIDs)	118	45	29	27	0	2	0	0	0	1	3	0	225
Hormones	115	99	9	7	1	0	2	0	0	0	4	0	237
Genital and reproductive organs	65	7	15	1	0	0	2	0	0	0	0	0	90
Dermatology	40	23	7	1	0	4	0	0	0	0	0	0	75
Digestive tract	47	41	29	12	0	2	2	0	0	0	0	0	133
Ocular and auricular products	61	32	0	0	0	0	0	0	0	0	0	0	93
Cardiovascular and circulatory system	67	33	9	6	0	0	0	0	0	0	0	0	115
Antineoplastic and immunomodulator agents	39	19	0	0	0	0	0	0	0	0	0	0	58
Blood and blood-forming organs	3	4	8	0	1	0	0	0	0	0	0	0	16
Respiratory system	7	2	2	5	0	0	0	0	0	0	0	0	16
Other	84	29	1	2	1	0	0	0	0	0	3	0	120
General total	**2448**	**1609**	**670**	**201**	**180**	**119**	**72**	**30**	**58**	**16**	**33**	**39**	**5475**

* The medicine category "Other" includes allergy products, homeopathic drugs and medicinal products for human use.

These breakdowns by species or therapeutic category were calculated on the basis of all the reports recorded in the national database, without taking into account the report typology or the conditions of use of the medicinal products (whether or not they complied with the summary of product characteristics – SPC).

Off-label uses of veterinary medicinal products traditionally account for a quarter of all reports. In 75% of cases, they are observed in cats (overdose, or use of permethrin, which is not authorised in this species) or dogs (overdose).

- MA amendments

The pharmacovigilance reports and their analysis, at either national or European level, enable the SPCs to be updated to include the new information obtained.

These amendments concerned 71 medicines in 2021, compared with 63 in 2020. The assessment of the pharmacovigilance data mainly led to the "Adverse events" section of the SPCs being updated, with the addition of new clinical signs or changes to their incidence, but also enabled new warnings, contraindications and precautions for use to be added.

These changes are made public via ANSES-ANMV's digital newsletter published on the ANSES website, to which readers can subscribe via anses.fr.

D2 – Communication on veterinary pharmacovigilance

In order to promote pharmacovigilance, ANSES-ANMV produces summaries of the reports recorded, related to a specific medicine, therapeutic category and/or species, and publishes position papers on ways to facilitate reporting and improve report quality. This information is disseminated via different media, such as the anses.fr website, the digital newsletter of the French Veterinary Association National Council (CNOV), the professional press and congresses.

In addition, ANSES-ANMV promotes research and thesis work in the field of veterinary pharmacovigilance by providing access to the data in the national pharmacovigilance database. Following the introduction of new provisions in favour of open science, in 2021 the Agency began placing "author versions" of articles it had published on both the institutional open archive site (HAL ANSES) and the Veterinary medicinal products page of the ANSES website, six months after their publication in journals.

- Articles and press releases

The articles published on pharmacovigilance in 2021 included a review of neurological adverse effects reported in dogs following the use of medicinal products containing metronidazole (*Le Point Vétérinaire* – Issue 413/414, January-February 2021), as well as two communications relating to a user risk identified for a pergolide-based medicinal product intended for horses, and for live attenuated vaccines administered intranasally to dogs. An article was also published in the pharmacy trade press to reiterate certain precautions concerning dog deworming, in particular because of certain breed particularities (*Le Moniteur des Pharmacies* – Issue 3391, November 2021), and two communications for the general public were published on the ANSES website, alerting to the risks of misuse of external antiparasitics in cats and rabbits. In 2021, the Agency also published an article on the pharmacovigilance data available in France and Europe on the use of alpha2-agonist anaesthetics in

Pomeranian dogs, in response to unsubstantiated rumours of particular breed sensitivity to these medicinal products.

Two articles also shared pharmacovigilance signals detected at European level with the general public. The first warned of possible adverse effects in pets due to their owners' topical hormone treatments (following the results of an investigation by the Swedish agency), while the second relayed information on the increased incidence of neonatal pancytopenia possibly caused by medication, in cattle in Belgium and the Netherlands.

Lastly, ANSES-ANMV continued the monthly publication of clinical cases in the *Dépêche Vétérinaire*, which began several years ago. Cases are selected for their potential interest to the veterinary profession. A description of each clinical case is supplemented by the pharmacovigilance specialist's analysis of the possible relationship between the administered medicine(s) and the clinical sign(s) observed subsequently, as well as the resulting causality score.

- Participation in congresses

ANSES-ANMV regularly discusses veterinary pharmacovigilance during its participation in professional events such as the national meetings of the veterinary technical groups (GTVs) and the annual congresses of the French Association of Veterinarians for Pets (AFVAC) and the French Equine Veterinary Association (AVEF).

In 2021, at the national congress of the AFVAC, the Agency presented a review of the adverse effects of medicinal products used for treating allergic dermatitis in dogs and cats, as well as the methodology for monitoring adverse effects through signal detection. A retrospective review of the adverse effects of internal antiparasitics based on ivermectin or moxidectin in Equidae was also presented at the AVEF congress last year, and a review of the lack of efficacy of medicinal products against varroa mites was presented at the *Journées Vétérinaires Apicoles* in Nantes.

- Internships

ANSES-ANMV regularly hosts trainees with a view to using pharmacovigilance data for veterinary doctoral theses. In 2021, an internship was carried out as part of a veterinary thesis in conjunction with the Epidemiological Surveillance Network for Equine Diseases (RESPE) and the National Veterinary School of Toulouse, on the subject of the lack of efficacy of influenza vaccines in horses. The results of this work will be presented at the next congress of the AVEF.

E/ Outlook for 2022

- Implementation of new European regulations

The legislative package to revise the EU regulations on veterinary medicinal products came into force on 28 January 2022. Adopted in December 2018 and published in January 2019, this legislative package consists of three texts:

- Regulation (EU) 2019/6 on veterinary medicinal products;
- Regulation (EU) 2019/4 on medicated feed;
- Regulation (EU) 2019/5 amending Regulation (EC) No 726/2004.

The main text concerns the regulations on veterinary medicinal products and aims to establish a single regulation throughout Europe to:

- safeguard public health, animal health and the environment;
- reduce the administrative burden;
- increase the availability of veterinary medicinal products;
- stimulate innovation.

This regulation on veterinary medicinal products provides for the publication of 27 secondary acts (9 delegated and 18 implementing acts). In order to prepare these secondary acts, the European Commission mandated EMA to provide scientific and technical opinions. ANSES-ANMV experts have been heavily involved, notably by chairing or co-chairing several of the groups working on this. The efforts of these groups, carried out on a tight schedule, led in particular to the validation of implementing acts on pharmacovigilance and on good distribution practices (for both finished products and active ingredients) in the second half of 2021.

At the same time, ANSES-ANMV was also involved in work on the IT tools to be developed, whether for:

- complying with the specifications of the European databases that ANSES-ANMV is required to update (in particular those on veterinary medicines and pharmacovigilance);
- adapting in-house tools for managing and monitoring the various dossiers to the new regulations.

Lastly, adaptation of French law to the various European texts will lead to changes in procedures, methodology and IT tools from 2022.

- Communication

Major efforts are being made to improve the information available on the Agency's website, with a complete overhaul of the ANSES site and its veterinary medicines portal. This new portal, which will come online in spring 2022, is intended to facilitate universal access to ANMV news and to the documents available on the various topics covered by the Agency.

F/ Summary and conclusions

As part of its post-MA surveillance activities, ANSES-ANMV conducted 72 inspections in establishments, representing 620 inspection days/missions.

Reports of quality defects, which have been generally stable in recent years, led to batch recalls in 23% of cases, while analytical controls of veterinary medicinal products found a 4.8% rate of non-compliance.

Shortages mainly concerned vaccines, mostly affecting dogs and cats. These shortages are the consequence of the strong market growth (+20%) due to the increase in the number of dogs and cats in French households. ANSES-ANMV is closely involved in managing these shortages, identifying alternatives when they concern critical medicines.

In pharmacovigilance, following two years of decline, the number of reports grew by 5% compared to 2020. The Agency is continuing its communication campaigns targeting professionals, in order to promote veterinary medicinal product pharmacovigilance.

2021 figures for post-MA activities

620 inspection days/missions
72 facilities inspected
91 reports of quality defects
18 batch recalls
145 analytical controls of medicines
83 stock shortages reported, including 9 critical
1718 advertising materials submitted
78 requests for classification (300 products)
4420 adverse effect reports

The main expectations for 2022 in the monitoring of veterinary medicinal products are fully in line with ANSES-ANMV's general activity programme and primarily concern two topics: the implementation of Regulation (EU) No 2019/6, which came into force on 28 January 2022, with, in particular, the adaptation of French regulations and ANSES-ANMV's IT tools to the European databases (especially those for medicinal products and pharmacovigilance); and communication, with the overhaul of the ANSES website and the veterinary medicines portal.

This seventh annual report on activities relating to post-MA surveillance of medicinal products shows that the quantitative results of this activity remain fairly consistent from one year to the next. These surveillance activities, carried out by ANSES-ANMV throughout the medicinal product lifecycle, help improve the safety of veterinary medicinal products.

GLOSSARY

- MA: Marketing authorisation
- GCP: Good clinical practices
- GDP: Good distribution practices
- GMP: Good manufacturing practices
- GLP: Good laboratory practices
- GAVPP: Good autonomous vaccine preparation practices
- CPVL: Veterinary Pharmacovigilance Centre in Lyon
- EMA: European Medicines Agency
- Non-EU GMP: Good manufacturing practice outside the European Union
- OMCL: Official medicines control laboratory
- SPC: Summary of product characteristics

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