FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS

2021 Annual Report

The French Agency for Veterinary Medicinal Products (ANMV), part of ANSES, is the competent authority for assessing and managing risks associated with veterinary medicinal products in France. It assesses national and European marketing authorisation (MA) applications for veterinary medicinal products, as well as European dossiers on acceptable maximum residue limits in foods of animal origin. It issues MAs for veterinary medicinal products and authorises clinical trials, imports and the temporary use of veterinary medical products. It authorises the opening of establishments for pharmaceutical manufacturing, licensed operation, wholesale distribution and export, and also certifies exports of veterinary medicinal products.

It monitors the risk of adverse effects and problems with market availability of veterinary medicinal products, verifies product quality and advertising, and inspects veterinary pharmaceutical establishments. Lastly, it is a collaborating centre for the World Organisation for Animal Health (OIE).

KEY FIGURES

Marketing authorisations (MAs)

74 MAs issued, 3 rapporteur missions for centralised procedures

1 dossier on maximum residue limits managed by ANSES-ANMV

741 import authorisations issued

Inspection and market surveillance

74 inspections of pharmaceutical establishments

544 quality control tests performed on 108 veterinary medicinal products

A SHIFTING CONTEXT

Adaptation for implementing the new European regulation on veterinary medicinal products

Regulation (EU) 2019/6, which is designed to **harmonise Member States' regulations and practices**, came into force on 28 January 2022. ANMV was a driving force during the drafting of the text, as well as in the three years preceding its entry into force, through its participation in and chairing of several working groups at both the European Medicines Agency (EMA) and the European Commission, with a view to drafting the texts specifying the implementation of the regulations.
Last year saw the adoption of four delegated acts and eight implementing acts for Regulation (EU) 2019/6, mainly concerning the collection of data on antimicrobials, good distribution and pharmacovigilance practices, and the product database.
ANMV has also offered new ideas on identifying the changes needed to national regulations, with preparation of the draft order, which was adopted in the first quarter of 2022.

Pharmacovigilance

4357

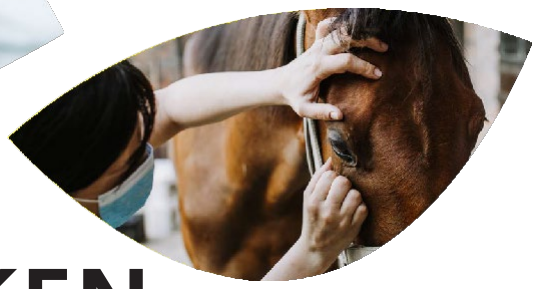
adverse effect reports registered, of which 2354 were considered serious

Preparatory work for the ANMV 2022-2026 roadmap

The previous roadmap ended in 2021. To prepare for the adoption of a new 2022-2026 roadmap, consultations were held internally, with a review of the reorganisation that took place in 2020, and externally, via questionnaires to our stakeholders. This roadmap takes into account the shifting European context, including the overhaul of the regulations and its significant impact at national level, changing working conditions with the recent ANMV reorganisation, and the consequences of the health crisis, which has led to widespread teleworking. The strategic goals of this roadmap concern the Agency's European and international role, and the development of major scientific fields such as the fight against antimicrobial resistance, and new therapies.
Following working groups with the active participation of staff and an Executive Board seminar, four main interacting themes were identified:
- improving the working environment;
- developing skills and adapting missions/resources;
- promoting ANMV;
- ANMV's digital transformation.

International activities performed remotely during COVID

ANMV's international activity was still heavily impacted by the health situation in 2021. However, some activity was maintained through virtual meetings, such as the training seminars held for OIE focal points for veterinary products in the European and American regions, which enabled the 6th cycle to be finalised.



WORK UNDERTAKEN AND KEY EVENTS

LAUNCH OF VIGIE: THE NEW NATIONAL PHARMACOVIGILANCE DATABASE

The steady increase in the number of reports of adverse events in recent years (+30% in 10 years) led ANMV to set up a national pharmacovigilance database that is more closely integrated into its overall information system.

This database, known as VIGIE, was commissioned in September 2021 to the great satisfaction of its users. VIGIE is a web application shared between ANMV and the Veterinary Pharmacovigilance Centre in Lyon (CPVL). It is interconnected with ANMV's veterinary medicines database and electronic submission website, and automatically forwards reports to the European network. These various developments significantly shorten the time taken to manage and monitor reports, and improve the security of information flows.

In terms of making best use of the data, the tool's numerous query possibilities and the introduction of an adapted signal detection tool will help improve ANMV's surveillance capabilities in this area.

ANSES'S CONTRIBUTION TO OPEN ARCHIVES

In 2020, ANSES and several other health agencies signed a joint declaration to promote open science, underlining their ambition to develop a joint approach for disseminating and sharing knowledge more widely.

ANSES systematically places "author versions" of articles on its institutional open archive site (HAL ANSES) six months after publication. These same versions are also published on the Veterinary Medicinal Products portal of its website.

This new dissemination method was introduced in April 2021 and concerned future articles written by or in collaboration with ANMV. At the same time, a total of 23 articles published in previous years were also made available online.

FALSIFIED VETERINARY MEDICINAL PRODUCTS

As part of its market surveillance activities, ANMV placed online orders on the *Wish* website for several antiparasitic collars which, according to the website visuals and descriptions, were SERESTO® collars authorised in France. After analysis in the ANMV laboratory, it turned out that they were falsified products from China containing no active ingredients. ANMV therefore published a communication on its website to warn users of the risks involved in purchasing falsified medicines online and their use; these range from the simple ineffectiveness of the product to potential toxicity for animals, humans and the environment associated with the hazardous substances these products may contain.

ANALYSIS OF COMBINATIONS OF MEDICATED PREMIXES CONTAINING ANTIMICROBIALS

Reporting of antimicrobial sales by manufacturers of medicated feedingstuffs helps identify how the compounds in question are used in livestock. The Monitoring Committee for Veterinary Medicinal Products, which reports to the Director of ANMV, used these data to study current knowledge about the physico-chemical and pharmacological interactions of these products, in order to determine their effects and confirm whether or not prescribing a combination of several medicated premixes is appropriate in the context of prudent and responsible use of antibiotic therapy.

USE OF VETERINARY MEDICINAL PRODUCTS IN BACKYARD POULTRY FLOCKS

More and more people are keeping laying hens in their gardens and eating their eggs. The owners often see these birds as pets.

Veterinarians are then faced with demands to treat these animals, despite limited availability of medicines in packaging tailored to small numbers of livestock. Prescribers also need to take into account the "food-producing" nature of these animals by not forgetting to specify, at the time of prescription, any action to be taken with regard to this produce and compliance with any withdrawal period necessary. The Monitoring Committee for Veterinary Medicinal Products has been working on this emerging issue by providing veterinarians with recommendations and a review of available therapies.

DEVELOPMENT OF EUROPEAN DATABASES

The new Regulation (EU) No 2019/6 on veterinary medicinal products provides for the creation of three databases:

- The "products" database contains information on veterinary medicinal products authorised in the European Union. ANMV co-chairs the group tasked with monitoring the IT project, which is being developed by the EMA in close collaboration with Member States. This database has been accessible since 28 July 2021, with the reference Member States responsible for initial data entry: France had thus transmitted data on more than 1518 products by the end of 2021.
- Eudravigilance Veterinary has been designed to receive all reports of suspected adverse events occurring in animals following the use of any medicinal products, or in humans following the use of veterinary medicinal products. ANMV contributes to the user working group by providing technical expertise to the IT developers and testing the tool.
- The database of establishments lists manufacturers and wholesale distributors of veterinary medicinal products. The pre-existing database has now been supplemented with additional information, such as wholesale distribution authorisations. ANMV is also a member of the working group for the development of this database.

PUBLICATION OF THE PHYTOTHERAPY OPINION

Given the growth in the use of herbal preparations (phytotherapy) and essential oils (aromatherapy) for medicinal purposes, ANSES issued an internal request to propose an assessment method suited to veterinary herbal medicines.

The aim was to define a list of plants for which there is no need to define maximum residue limits because their use is considered safe for consumers, taking into account the data available in other areas (plants normally consumed by animals or humans, plants used in food supplements or medicines for human use, and plants that are not toxic to humans at the doses used). The proposed methodology also helped identify certain plants or parts of plants for which there was a lack of studies or data, meaning that it was not possible to conclude as to an absence of concern. Nevertheless, some plants cannot be used in veterinary medicine due to their proven toxicity to humans and a possible risk to consumers.

Work is continuing with the establishment of an ANSES working group including veterinary medicinal products and the raising of awareness at European level, with the organisation of a conference as part of the French Presidency of the Council of the European Union.

OUTLOOK AND PROJECTS INITIATED

REVISION OF NATIONAL REGULATIONS

The European regulations that are directly applicable in the Member States have a major impact on national regulations, since many points are now defined in the European regulation thereby leading to the deletion of numerous articles in the French Public Health Code.

Act No. 2020-1508 of 3 December 2020 allows the government to legislate by issuing an order within 16 months to adapt national regulations to European Union law.

ANMV spearheads proposals for analysing the amendments and additions needed to comply with EU law. The draft order is being prepared in consultation with the General Directorate for Health (DGS), the General Directorate for Food (DGAL) and ANMV with a view to publication in the first quarter of 2022. These legislative amendments will be followed by the adoption of implementing decrees.

ANTIMICROBIAL RESISTANCE

ANMV is taking part in the management of a project seeking solutions to the unavailability of certain antibiotics. This three-year project aims to identify the root causes of the shortages and lack of availability in France of antibiotics whose patents have fallen into the public domain (in human and animal health, while also taking the environment into account) and propose effective solutions, in line with the "One Health" approach. The PARS project is being funded by the EU through the Technical Support Instrument (TSI) and implemented by the WHO in cooperation with the European Commission's Directorate-General for Structural Reform Support (DG REFORM).

The first phase of this project (November 2020 to December 2021) sought to analyse antibiotic shortages and lack of availability in human and veterinary medicine.

This will help identify the root causes of supply-chain disruptions and availability problems in the human and veterinary sectors. Lastly, possible measures to address these root causes will be proposed.

ANMV's INTERNATIONAL WORK

INTERNATIONAL ACTIVITIES PERFORMED REMOTELY DURING COVID

ANMV 's international activity was still heavily impacted by the health situation in 2021. However, some activity was maintained through virtual meetings, such as the training seminars held for OIE focal points for veterinary products in the European and American regions, which enabled the 6th cycle to be finalised.

DEVELOPMENT OF A DISTANCE-LEARNING MODULE ON AUTOGENOUS VACCINES

ANMV and the French National School of Veterinary Services (ENSV) in Lyon have prepared an online training module on the analysis of risks associated with inactivated bacterial autogenous vaccines and the implementation of regulatory measures to control them. This training is one of the recommendations adopted at the Second OIE Global Conference on antimicrobial resistance in 2018. This training is intended for veterinary services experts involved in implementing regulations, assessing risks and verifying autogenous vaccines. ANMV contributed its expertise on autogenous vaccines. This module was launched on Tuesday 16 November 2021 with 14 participants.

Shortages of veterinary medicinal products

Since 2018, ANMV has issued a communication on its website during each critical shortage guiding veterinary practitioners towards possible alternatives. This is then updated according to new information received and any changes to the situation. A feedback campaign among stakeholders was recently conducted.

The good practice guide for managing shortages and the form for reporting and monitoring shortages have been revised to account for the updated status of ongoing shortages and to include in the management methods the release of specific batches by ANMV. Imports and temporary use authorisations for medicines authorised in other countries are also key measures for addressing shortages.

An increase of about 20% was noted compared to 2019, possibly related to the health crisis. Vaccines, accounting for 27%, led the reported shortages, followed by anti-inflammatory drugs (17%) and antibiotics (15%). The vaccine shortages are due to supply difficulties in the pet market, which has been growing sharply since 2020. Among the anti-inflammatories, meloxicam-based medicines (in various forms) were particularly affected, while the main antibiotics concerned were those based on amoxicillin (+ clavulanic acid).

Introduction of electronic signatures

As part of its sustainable development policy and to support the new work organisation, ANMV is pursuing its project to digitise its processes. Users can send their applications to ANMV electronically by depositing them on the Common European Submission Platform (CESP).

ANSES has also introduced an electronic signature tool that was deployed from July 2021 for decisions relating to veterinary medicinal products. Signed decisions are transmitted to the applicant electronically (sent by email to an institutional address).

Communication with stakeholders: ANMV took an active part in the annual congresses of the veterinary profession

The Agency's involvement focused on the work of ANMV, particularly in the areas of pharmacovigilance and antimicrobial resistance, as well as the numerous regulatory developments due to the revision of the European framework. These congresses provided an opportunity for discussions with veterinarians and enabled feedback to be obtained on the problems of using veterinary medicines in the field. In 2021, ANMV participated in three main congresses:

National meeting of the veterinary technical groups (JNGTV), which brought together 302 "rural" practitioners. Three ANMV employees gave presentations on pharmacovigilance and on the use of veterinary medicines in beekeeping.

The French Equine Veterinary Association (AVEF) event attracted 303 "equine" practitioners. ANMV gave a presentation on pharmacovigilance.

The French Association of Veterinarians for Pets (AFVAC) brought together 2418 "canine" practitioners. Six presentations were given by ANMV staff on pharmacovigilance and changes in regulations.

Third ANMV Day

On 12 October, ANMV organised its third meeting for all its stakeholders representing the entire veterinary medicine chain. 150 people attended via videoconference.

The event focused on the entry into force of the Veterinary Medicinal Products Regulation, with presentations on the work carried out by the EC and the EMA, and the efforts of ANMV in this regard. Three short presentations concerned a demonstration of the EU product database, the online sale of veterinary medicines and rules for the oral administration of veterinary medicines.

The afternoon was devoted to workshops detailing the impact of the European regulations on marketing authorisation procedures, veterinary pharmacovigilance, good distribution practices and management of veterinary pharmaceutical establishments, as well as their impact on national law, in collaboration with the technical offices of the General Directorate for Health and the General Directorate for Food.

The efforts of the French Agency for Veterinary Medicinal Products and the technical teams ensured that the day was a great success.

MAIN PUBLICATIONS

CHEVANCE, A., URBAN, D. and MOULIN, G.
Cessions d'aliments médicamenteux contenant des antibiotiques en France. Résultats pour l'année 2020 Anses ANMV

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Contextes sanitaire et économique en médecine vétérinaire et utilisation d'antibiotiques en France en 2020 Bulletin épidémiologique - santé animale-alimentation, vol: n°: 92, p: 1-8

MAYTIE, B., BASTIEN, J., MOULIN, G., GRISOT, L. and GRACH, G.
Expression des doses en UI ou en mg des antibiotiques : exemple de la gentamicine
Dépêche technique (la), vol: n°: 187, p: 14-14

MAYTIE, B., GRISOT, L. and BADUEL, L.
Modalités pratiques et contraintes de l'emploi des fasciolicides en conditions terrain
Dépêche technique, vol: n°: 181, p: 21-27

PIQUEMAL, C. and LAURENTIE, S.
Mortalité suite à l'application d'un spot on associant imidaclopride et sélamectine chez des canaris: quel est votre avis ?
Dépêche vétérinaire (la), vol: n°: 1563, p: 15-15

ROUGIER, S., BÉGON, E., DEMAY, F. and LAURENTIE, S.
Prascend pour chevaux : alerte sur des cas d'ingestion humaine accidentelleDépêche vétérinaire (la), vol: n°: 1563, p: 8-8

ROUGIER, S., BÉGON, E., DEMAY, F. and LAURENTIE, S.
Vaccins intranasaux contre la toux de chenil : des précautions d'emploi pour éviter toute contamination humaine
Dépêche vétérinaire (la), vol: n°: 1570, p: 13-13

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Vaccination et déficit proprioceptif chez un chien : quel est votre avis ?
Dépêche vétérinaire (la), vol: n°: 1570, p: 14-14

BIÉTRIX, J., BÉGON, E., DEMAY, F. and LAURENTIE, S.
Usage des anesthésiques alpha2-agonistes chez le spitz nain : pas de contre-indication particulière chez les chiens en bonne santé
Dépêche vétérinaire (la), vol: n°: 1577, p: 16-16

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Imidocarbe et tachycardie, tachypnée, mydriase chez un chien : Quel est votre avis ?
Dépêche vétérinaire (la), vol: n°: 1578, p: 24-24

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Dépêche vétérinaire (la), vol: n°: 1580, p: 20-20

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Traitement hormonaux cutanés chez l'homme : des effets indésirables chez l'animal de compagnie
Dépêche vétérinaire (la), vol: n°: 1596, p: 20-20

BURONFOSSE-ROQUE, F. and LAURENTIE, S.
Défaut d'efficacité lors d'avortement provoqué chez la chienne : trop de précautions valent mieux que pas assez
Dépêche vétérinaire (la), vol: n°: 1598-1599, p: 15-15

KEY DATES

28 JULY — *European product database launched* → **13 SEPTEMBER** — *VIGIE launched* → **12 OCTOBER**

PIQUEMAL, C., BÉGON, E., DEMAY, F. and LAURENTIE, S.
Pancytopénie néonatale bovine : penser aux traitements administrés à la mère
Dépêche vétérinaire (la), vol: n°: 1598-1599, p: 21-21

ROUGIER, S. and LAURENTIE, S. Traitement intra-mammaire et présence d'inhibiteurs dans le lait malgré un temps d'attente respecté: Quel est votre avis ?
La dépêche vétérinaire, vol: n°: 1557, p: 22-22

PIQUEMAL, C. and LAURENTIE, S.
Sédation prolongée suite à l'induction de vomissements chez un chat : quel est votre avis?
La dépêche vétérinaire, vol: n°: 1584, p: 16-16

PIQUEMAL, C. and LAURENTIE, S.
Décès et avortements de brebis suite à un traitement à base de moxidectine : quel est votre avis ?
La dépêche vétérinaire, vol: n°: 1586, p: 22-22

MORICEAU, M.-A. and LAURENTIE, S.
Mortalité et nécrose auriculaire suite à un traitement au lévamisole chez des porcelets
La dépêche vétérinaire, vol: n°: 1590, p: 26-26

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Vermifugation du chien et particularités raciales
Le moniteur des pharmacies, vol: n°: 3391, p: 34-34

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Pharmacocinétique et efficacité clinique du tramadol chez le chien
Nouveau praticien vétérinaire canine-féline, vol: n°: 77, p: 61-63

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Point vétérinaire (le), vol: n°: 413, p: 50-55

BADUEL, L.
Les gaps thérapeutiques en filière animaux de compagnie: le rôle de l'Agence Nationale du Médicament Vétérinaire (ANMV). Tribune Pratique vétérinaire, vol: n°: 191, p: 5-5

CARNAT-GAUTIER, P.
Legacy data migration
TOPRA Veterinary medicines symposium, 22-23/09/2021, Online

BIÉTRIX, J., MORICEAU, M.-A. and LAURENTIE, S.
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Vigil'Anses, vol: n°: 13, p: 14-18

BIETRIX, J. and LAURENTIE, S.
Les médicaments antiparasitaires pour chiens et chats à base de fipronil ne doivent pas être appliqués aux lapins
Vigil'Anses, vol: n°: 14, p: 1-3

ROUGIER, S. and LAURENTIE, S.
Comprimés de Prascend pour chevaux : attention au risque d'ingestion accidentelle et mesure de précaution à prendre en cas d'accident
Vigil'Anses, vol: n°: 15, p: 11-14

MOULIN, G.
Figth against antimicrobial resistance.The French experience
Webinar OIE-GNKI, 18-11-2021, Online

Third ANMV day → **16 NOVEMBER** *International distance-learning module on autogenous vaccines* → **27 NOVEMBER** *Export of data on existing medicines to the European product database*

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