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French agency for food, environmental and occupational health & safety

Investigate, evaluate, protect

2019 ANNUAL REPORT

FRENCH AGENCY FOR VETERINARY MEDICINAL PRODUCTS

Entity

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, authorises clinical trials, imports, temporary use and the opening of establishments for pharmaceutical manufacturing, 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).

"The French Agency for Veterinary Medicinal Products verifies product quality and advertising, and inspects veterinary pharmaceutical establishments."

SECOND ANMV DAY: A MEETING WITH STAKEHOLDERS

On 15 October 2019, the ANMV organised its second one-day meeting with 100 people representing all its stakeholders in the veterinary medicinal product line: veterinary pharmaceutical manufacturers, wholesale distributors, veterinarians, livestock farmers and OIE representatives. The morning saw presentations on the latest developments in the new veterinary regulations, the legal status of veterinary medicinal products and borderline products, and a review of the revision of withdrawal periods. The presentations were interspersed with brief items on Brexit impact and veterinary medicinal product advertising, and an update on work on the impact of biocidal products on veterinary drug distribution in drinking water. The afternoon was devoted to workshops on "Antibiotic use: what indicators? For what purposes?"; "Twenty years of pharmacovigilance: what expectations and outlook for veterinary pharmacovigilance?" and "The Advisory Committee for Veterinary Medicinal Products: assessment of its first term and reflection on the orientations and prospects for its second term". This very full day gave each stakeholder a chance to exchange ideas and identify promising areas of work to be explored.

Context

At the European level, 2019 was mainly characterised by:

- the entry into force of the legislative package relating to veterinary medicinal products, comprising three European regulations. This was followed by the start of work on adopting the delegated and implementing acts necessary for its application, through the establishment of expert working groups at the European Medicines Agency (EMA) in which the ANMV participated, and negotiation meetings at the European Commission. At the same time, EMA and the European Commission also set up expert groups to develop the databases and IT tools provided for in the regulations;
- the continuation of preparatory work for the implementation of Brexit, in particular a study of the impact of a no-deal UK withdrawal on the availability of veterinary medicinal products in France;

"In 2019, the ANMV also underwent some structural changes, with the move to its new premises and an overhaul of its organisation."

KEY FIGURES

MARKETING AUTHORISATIONS MAS

95 MAs issued

761 import authorisations issued

INSPECTION AND MARKET SURVEILLANCE

68 inspections of pharmaceutical establishments

352 quality control tests performed on **89** veterinary medicinal products

PHARMACOVIGILANCE

4,606 adverse effect reports recorded, of which **2,428** were considered serious

Work undertaken and key events

WORK IN VETERINARY PHARMACOVIGILANCE

In 2019, veterinary pharmacovigilance work carried out as part of a thesis defence was finalised. Based on retrospective studies of declarations, this work focused on the nephrotoxicity of veterinary medecines in dogs and cats and serious side effects of vaccines in cats. A study was also conducted on post-vaccinal events in horses reported over a three-year period (2016-2018).

In 2019, the ANMV issued calls for vigilance when using veterinary medicines containing altrenogest for humans, as well as a reminder of the serious secondary risks of administering permethrin to cats, which should be avoided at all costs.

"For the first time in France, an eprinomectin resistant Trichostrongylus/ Teladorsagia population has been detected"

EPRIBELE

In connection with a call for expressions of interest (EPRIBELE project), a veterinary thesis on a method for detecting suspected inefficacy of eprinomectin administered topically to dairy goats was defended in October. The experimental study conducted on six dairy goat farms detected an eprinomectin-resistant *Trichostrongylus/Teladorsagia* population for the first time in France, and proposed a method for detecting the inefficacy of eprinomectin in dairy goats with the help of a faecal egg-count reduction test that can be used to document cases for pharmacovigilance.

CONTRIBUTION TO THE TEXTS OF THE EUROPEAN PHARMACOPOEIA

In June, the European Pharmacopoeia Commission adopted 43 monographs and chapters by the group of experts in charge of veterinary vaccine monographs (15V) subsequent to implementation of a new approach to managing foreign agents in immunological veterinary medicinal products. This work was carried out over six years in conjunction with EMA's Immunology Working Party (IWP), in a context of international harmonisation (VICH). The ANMV has chaired the 15V group for the past eight years. 15V is tasked with drafting and revising the European Pharmacopoeia's monographs and chapters on veterinary vaccines and immunosera.

EU-US AGREEMENT ON MUTUAL RECOGNITION: THE ANMV AUDITS THE FDA

From 10 to 14 June 2019, the ANMV conducted an audit of the US Food and Drug Administration (FDA), mandated by the European Commission. The audit team consisted of three inspectors from Italy, Germany and Poland, led by the head of the ANMV's Inspection Unit. This audit took place as part of the extension of the Agreement on mutual recognition between the European Union and the United States to include the veterinary field. The Agreement concerns inspections carried out on drug manufacturing sites in the respective territories. This major agreement between the EU and the FDA updates the historic 1998 text and strengthens relations on both sides of the Atlantic, with a view to better streamlining the resources devoted to inspections and deploying more resources to other regions of the world where active substances and medicines are produced. As a result, US inspectors will no longer have to come to inspect veterinary drug manufacturing establishments located in the European Union for exports to the United States. This agreement will increase access to high-quality, safe and effective medicines regardless of where they are manufactured and will make it easier to prioritise inspections of the highest risk sites.

"These data enable a more accurate assessment of antimicrobial use in different animal species receiving antimicrobials in medicated feed"

WORK ON ANTIMICROBIAL RESISTANCE

As part of the mandatory reporting of antimicrobial sales by retailers of veterinary medicinal products, in July 2019 the ANMV published its first report providing an initial analysis of the data supplied by manufacturers and distributors of medicated feed. These data enable a more accurate assessment of antimicrobial use in different animal species receiving antimicrobials in medicated feed.

The ANMV played an active role in European work on antimicrobial resistance, in particular on the categorisation of antimicrobials (Antimicrobial Expert Group – AMEG) and on the delegated acts provided for by the new European regulations (collection of usage data, establishment of the list of antimicrobials reserved for human use only).

Further afield, the ANMV continued to participate in international groups working on the subject: OIE Working Group on Antimicrobial Resistance, United Nations InterAgency Coordination Group, Codex Alimentarius Task Force on Antimicrobial Resistance.

SUSTAINED ANMV ACTIVITY ON THE INTERNATIONAL SCENE

As an OIE Collaborating Centre for Veterinary Medicinal Products, the ANMV contributed its expertise particularly in the field of antimicrobial resistance by participating in the Working Group's activities during the general session in May, as well as in development of the antimicrobial use surveillance database. In addition, 2019 saw the launch of the sixth training cycle for OIE national focal points for veterinary products, on the topics of veterinary medicinal product quality, pharmacovigilance and autogenous vaccines. Besides supporting the drafting of this cycle's scientific programme, the ANMV took part in the first two meetings held: one in Addis Ababa (Ethiopia) for English-speaking African countries, and the other in Lomé (Togo) for French-speaking African countries.

Under the bilateral agreements it has signed, the ANMV received a delegation from the China Institute of Veterinary Drug Control (IVDC) in 2019, in order to take stock of their cooperation agreement, which will be renewed for a further five-year period starting in 2020. The Agency also hosted Chinese experts for training on several topics. Lastly, exchanges with Thailand continued this year on the themes of drug quality control, antimicrobial resistance and autogenous vaccines.

"The exchanges with Thailand continued this year on the themes of drug quality control, antimicrobial resistance and autogenous vaccines."

THE ANMV MOVES INTO NEW PREMISES AND RESHUFFLES ITS ORGANISATION

The ANMV moved into its new premises at the heart of the Bio-Agropolis centre of excellence in Javené, near Fougères, on 1 April 2019. The building was inaugurated on 23 May 2019 in the presence of Roger Genet, Director General of ANSES; Loïg Chesnais-Girard, President of the Brittany Regional Council; Jean-Luc Chenut, President of the Ille-et-Vilaine Departmental Council; and Jean-Pierre Orand, Director of the ANMV.

In order to meet the new challenges facing the Agency and rebalance the different core departments, the ANMV decided to reorganise its structure around three core departments and three units:

→ A Scientific Assessment Department, a Licensing Department and an Inspection, Market Surveillance & Pharmacovigilance Department;

→ A European & International Affairs Unit, a Regulatory Affairs & General projects Unit and an Antimicrobial Resistance Unit.

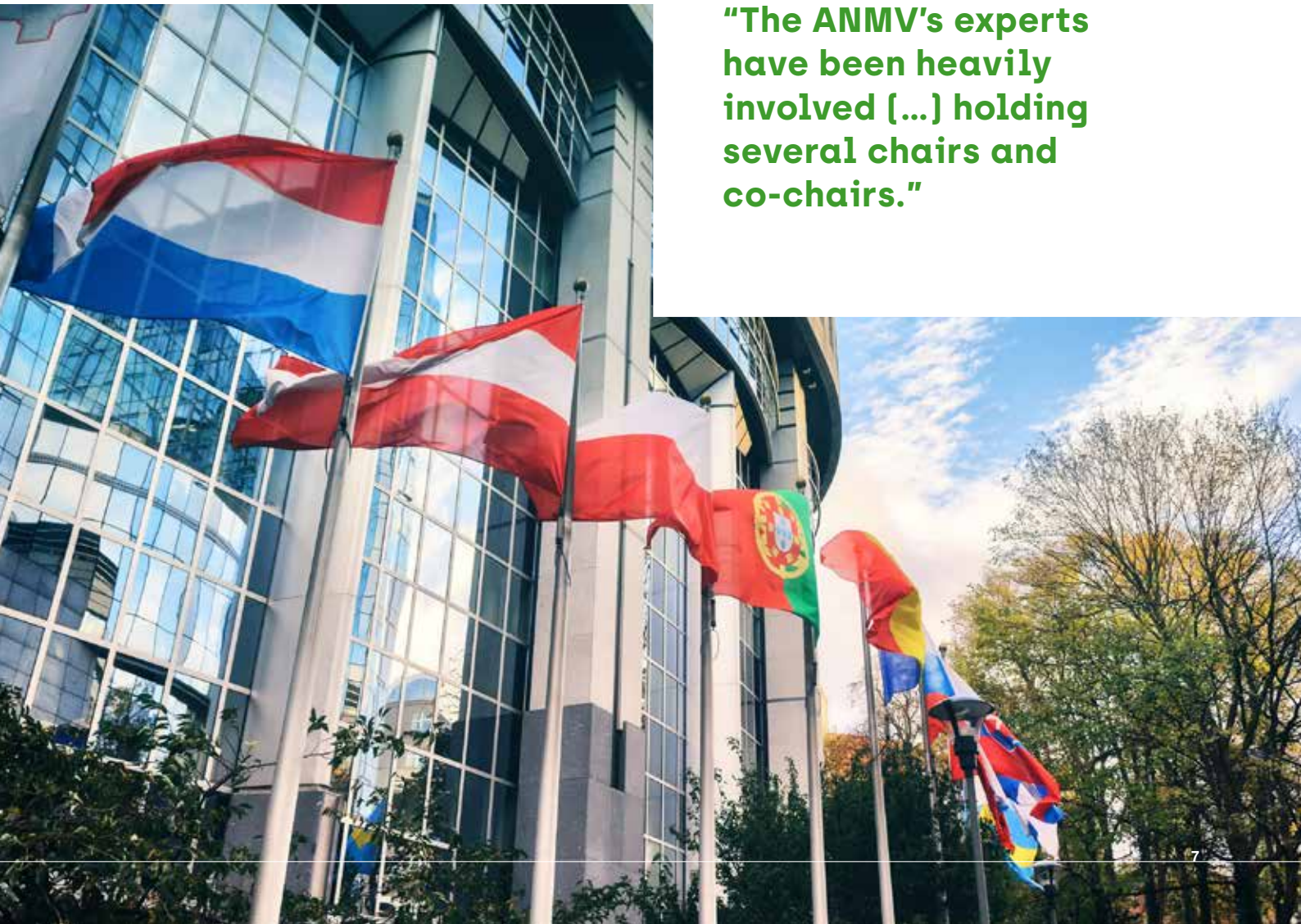
This restructuring has enabled risk assessment to be better segregated from risk management, as is the case for other regulated products within ANSES's Regulated Products Division.

Outlook and projects initiated

IMPLEMENTATION OF THE NEW EUROPEAN REGULATIONS

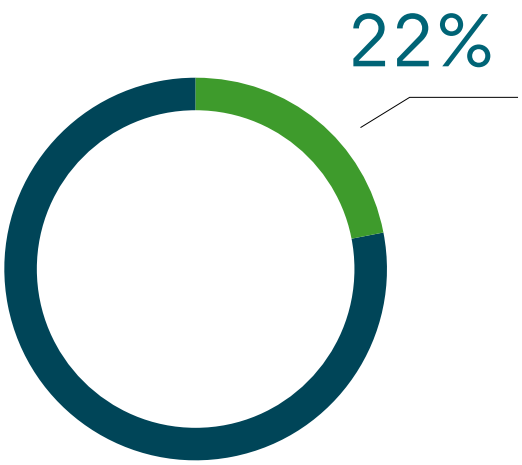
The European regulations on veterinary medicinal products and medicated feed provide for numerous delegated and implementing acts. In order to prepare these secondary acts, the European Commission mandated EMA to provide scientific and technical opinions. The work has been divided into four packages according to the adoption deadlines set out in the regulations. In 2019, five working groups issued recommendations on the acts to be adopted before the Regulation comes into force, and eight groups started or are continuing their work on the draft acts to be adopted upon its entry into force. The ANMV's experts have been heavily involved in these groups, holding several chairs and co-chairs. The ANMV is also supporting its supervisory ministries at meetings with the European Commission, and has been involved in the proofreading of draft acts.

"The ANMV's experts have been heavily involved (...) holding several chairs and co-chairs."



PREPARING FOR BREXIT

After 29 March 2017, the date on which the United Kingdom announced its intention to leave the European Union, the ANMV adopted an action plan in order to strengthen its position within European bodies and the network of agencies, mainly through a plan to bolster its teams. In 2019, the ANMV continued to work with MA holders whose dossiers did not yet comply with European regulations, in order to reduce Brexit's impact on the availability of veterinary medecines in France. The ANMV is now the Reference Member State for 139 mutual recognition and decentralised procedures previously managed by the United Kingdom, i.e. for 22% of them.



"The ANMV is now the Reference Member State for 139 mutual recognition and decentralised procedures previously managed by the United Kingdom."

RENEWAL OF THE ADVISORY COMMITTEE FOR VETERINARY MEDICINAL PRODUCTS

ANSES issued a call for candidates to renew the Advisory Committee for Veterinary Medicinal Products for a second term until 2022. The Committee is tasked with providing ANSES and the ANMV with a cross-cutting view of the issues in the field that they could take into account when making administrative decisions, in order to better manage the risks associated with veterinary medicinal products. It therefore provides information and is consulted on optimising the pharmacovigilance system, mainly in connection with the promotion, collection and sharing of signals detected in this framework, the safe use of products with regard to human and animal health and the risk to the environment, the conditions of applicability of risk management measures with regard to marketing authorisations, problems of veterinary drug availability, and its contribution to the identification of priority topics for expert appraisals or studies to be conducted on veterinary medicinal products, and how they are checked and monitored.

OFFICIAL MEDICINES CONTROL LABORATORIES AUDIT

The ANMV Control Laboratory, which is part of the European Network of Official Medicines Control Laboratories (OMCLs), received a team of two auditors from 2 to 4 July 2019 as part of the Mutual Joint Audit conducted by the European Directorate for the Quality of Medicines and Healthcare (EDMQ). This audit covered the scope of veterinary drug quality control and, in particular, compliance with the ISO 17025 standard and OMCL guidelines. The team consisted of an auditor from the Austrian OMCL and an auditor from the EDQM, the organisation that oversees the OMCL network. The results of this audit led to the renewal of recognition by the OMCL network. This audit highlighted the ANMV's work and the robustness of its quality system.

WORK ON THE UNION PRODUCT DATABASE (UPD)

The development of a common database of veterinary medicinal products in the EU is enshrined in Regulation (EU) 2019/6. EMA's expert group, chaired by an expert from the ANMV, issued in late August 2019 its recommendations for the establishment of this database. To ensure that it is interoperable and interconnected with other European databases and tools, this database will use the referentials and organisations of the programme to overhaul the European drugs databases (SPOR), and will be the reference database for information on veterinary medicinal products. The ANMV is closely involved in the governance of these projects at EMA level.

1 APRIL

→ Move into the new ANMV building

10 TO 14 JUNE

→ US FDA inspection, led by an ANMV inspector, as part of preparation for EU-US mutual recognition agreements

MAIN PUBLICATIONS

→ VAN DUIJKEREN, E., SCHWARZ, C., BOUCHARD, D., CATRY, B., POMBA, C., BAPTISTE, K.E., MORENO, M.A., RANTALA, M., RUZAUSKAS, M., SANDERS, P., TEALE, C., WESTER, A.L., IGNATE, K., KUNSAGI, Z. and JUKES, H.; The use of aminoglycosides in animals within the EU: development of resistance in animals and possible impact on human and animal health: a review; Journal of antimicrobial chemotherapy

→ GOCHEZ, D., RAICEK, M., PINTO FERREIRA, J., JEANNIN, M., MOULIN, G. and ERLACHER-VINDEL, E.; OIE Annual Report on Antimicrobial Agents Intended for Use in Animals: Methods Used; Frontiers in veterinary science, vol: 6, n°: p: 317

→ CARIA, M., ROUGIER, S., BEGON, E., FRESNAY, E., MALLEM, Y. and LAURENTIE, S. ; Néphrotoxicité des médicaments vétérinaires: étude rétrospective des cas de pharmacovigilance déclarés chez le chien et le chat ; Le point vétérinaire rural, vol: n°: 396, p: 21-21

→ BADUEL, L., COURTY, B., HARVEY, M., JACQUES, A.-M., LOUET, S. and REDUREAU, M. ; Evolutions des temps d'attente dans le cadre de l'AMM: motivations et impacts ; Bulletin des GTV, vol: n°: 95, p: 77-80

→ BEGON, E. and LAURENTIE, S. ; Doxycycline et gobage de mouches chez un chien: quel est votre avis?; Dépêche vétérinaire (la), vol: n°: 1488, p: 34-34

→ BURONFOSSE, F. and LAURENTIE, S.; Ataxie post-partum après euthanasie des chiots: quel est votre avis? ; Dépêche vétérinaire (la), vol: n°: 1477, p: 18-18

2 TO 4 JULY

→ Audit for renewal of accreditation by the European network of Official Medicines Control Laboratories (OMCLs)

28 SEPTEMBER

→ Renewal of the members of the Advisory Committee for Veterinary Medicinal Products

15 OCTOBER

→ Second ANMV Day

→ CARNAT-GAUTIER, P.; Trois questions à Paule Carnat-Gautier, chef de la Mission des affaires juridiques et du contentieux de l'Agence nationale du médicament vétérinaire. «Ce texte démontre que le vétérinaire français s'inscrit dans un contexte européen.»; Semaine vétérinaire (la), vol: n°: 1791, p: 12-12

→ GUICHARD, P., BORDAS, A., MORÉAC, T., CHEVANCE, A., BLOT, J., TRAVEL, A., HEMONIC, A., LENORMAND, B., LIBER, M., LEORAT, J., VERDON, J., HURTAUD-PESSEL, D., ORAND, J.-P., AMAR, H., MARIS, P., BADUEL, L. and MOMPELAT, S.; Impact du traitement par les biocides des eaux d'abreuvement des porcs, des volailles et des lapins sur la stabilité des antibiotiques ; Bulletin des GTV, vol: n°: 96, p: 49-55

→ FRESNAY, E., LAURENTIE, S. and PETTI, G. ; Mieux utiliser les médicaments avec la pharmacovigilance ; Réussir pâtre, vol: n°: 664, p: 29-30

→ MORICEAU, M.-A. and LAURENTIE, S. ; Spinosad et troubles comportementaux puis nerveux: quel est votre avis?; Dépêche vétérinaire (la), vol: n°: 1502-1503, p: 26-26

→ LAURENTIE, S. ; Altrenogest: des médicaments vétérinaires à utiliser avec précaution ; Vigil'Anses, vol: n°: 9, p: 1-2

→ 2018 Sales Survey of Veterinary Medicinal Products containing Antimicrobials in France; Delphine URBAN, Anne CHEVANCE and Gérard MOULIN, ANSES-ANMV – Scientific publication; ANSES – French Agency for Veterinary Medicinal Products

→ 2018 Annual Report on Post-MA Surveillance; Jean-Pierre ORAND, Mickaëlle SACHET, Sylviane LAURENTIE, Gregory VERDIER, Flore DEMAY, Nathalie LEGRAND, Delphine BARBOT; ANSES-ANMV – Scientific publication; ANSES – French Agency for Veterinary Medicinal Products

→ Sales of medicated feedingstuffs containing antimicrobials in France. Analysis of the results for the first two quarters of 2018; CHEVANCE, A., URBAN, D. and MOULIN, G.; ANSES-ANMV/Assessment of Chemical Veterinary Drugs Unit//Market Surveillance Unit

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