EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Veterinary pharmacovigilance 2017

Public bulletin

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

14 March 2018
EMA/697615/2017
Committee for Medicinal Products for Veterinary Use

Veterinary pharmacovigilance 2017

Public bulletin

1. Executive Summary

This public bulletin is aimed at informing veterinarians and the public of the main outcome of pharmacovigilance[1] or post-marketing surveillance activities for veterinary medicinal products (VMPs) during 2017 at the European Medicines Agency (EMA). The bulletin summarises recommendations to amend safety warnings and highlights ongoing monitoring of several centrally authorised products (CAPs[2]). A summary of the discussions and agreements at European level by the Pharmacovigilance Working Party (PhVWP-V) regarding pharmacovigilance issues concerning nationally authorised VMPs is also included.

The post marketing surveillance of CAPs has been further strengthened through an overall increase in adverse event reporting and the availability of these reports from a single central European Union (EU) database called EudraVigilance Veterinary (EVVet).

It is essential to emphasise the importance of the contributions made by veterinarians as they are the primary reporting source for adverse events, in addition to the efforts made by animal owners, handlers and farmers. The adverse event reports that are initially reported to either the marketing authorisation holder (MAH) or the regulatory authority are collected in the European central database, together with adverse event reports originating from outside the EU on the same or similar products. The reporting of adverse events by veterinarians remains the pre-dominant route for regulators to follow-up on the safety and efficacy of VMPs once these are marketed. Veterinarians are encouraged to continue reporting directly to their local regulatory authority[3] or to the MAH. It is acknowledged that there is a need to improve and increase communication and feedback on pharmacovigilance findings to veterinarians and this has been included as a priority in the CVMP and PhVWP-V work plans for 2018.

[1] Pharmacovigilance relates to any adverse events potentially linked to the use of a VMP, including possible lack of efficacy, environmental problems and investigations of the validity of the withdrawal periods.
[2] These are VMPs that are authorised through the centralised marketing authorisation procedure operated by the European Medicines Agency.
[3] In some Member States reporting to the regulatory authority is mandatory for veterinarians.

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

2. Introduction

This is the 15th public bulletin from EMA on veterinary pharmacovigilance activities, covering the year 2017. The aim of this bulletin is to contribute to the public communication on VMPs, particularly on the surveillance of adverse events and safety issues of veterinary medicines in the EU.

All adverse event reports occurring in the EU reported after the use of authorised VMPs are collected and evaluated both by the MAH, who is responsible for the product, and by the national competent authorities and/or EMA. These reports may be classified as “serious”, including events such as death, life-threatening reactions or permanent lesions and reactions resulting in significant disability or incapacity in the treated animal(s). Adverse events in humans handling the veterinary medicinal product are also classed as “serious”. In addition to the reporting of all adverse event reports occurring in the EU, the MAH is obliged to report serious and unexpected adverse event reports occurring outside the EU, when the product concerned is also authorised in the EU.

Electronic reporting became mandatory in November 2005 for serious reports only which are collated in the single EU database, EVVet. EVVet now contains 253,008 reports of adverse events[4], approximately 56% of which occurred within the EU/EEA and 44% outside the EU/EEA.

The overall surveillance of adverse events is carried out predominantly using two processes:

1) Periodic safety update reports (PSURs), which are a review of all adverse event reports having occurred in a set period, are compiled by the MAH and submitted to the responsible authority for review at defined time points.

2) Continuous monitoring of all pharmacovigilance data as it becomes available is conducted via signal detection by national competent authorities and the EMA.

Under the current EU legislation, the EMA Committee for Medicinal Products for Veterinary Use (CVMP) and its PhVWP-V are responsible for the pharmacovigilance of centrally authorised VMPs i.e. the products that have been granted an EU-wide marketing authorisation, whereas the surveillance of non-centrally authorised VMPs is undertaken by the competent authorities at Member State level.

[4] One report can contain more than one animal affected, especially in food producing animals. See Table 1 in the annex for further detail on the number of reports/number of animals affected broken down by species (including humans).

3. Adverse events in animals and humans involving centrally authorised products

There are now 192 VMPs that have been authorised via the centralised procedure since 1995 and which have marketing authorisations valid across the entire EU. An overview of the products and detailed information on each product, including the summary of product characteristics, is accessible on the EMA website (http://www.ema.europa.eu/ema/).

A total of 26,598 adverse event reports relating to exposure to centrally authorised products were received in 2017. Of these, 25,890 adverse event reports related to animals and 708 adverse event reports related to humans exposed to a veterinary medicinal product.

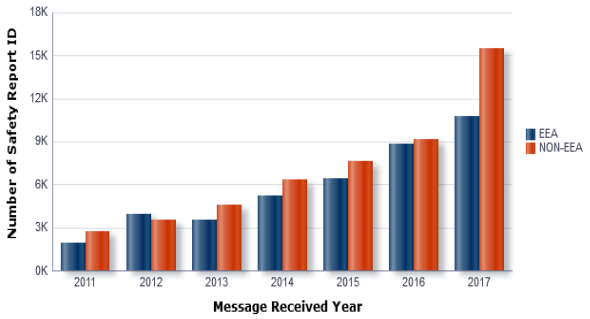


Figure 1. Total number of adverse events for centrally authorised products reported to EVVet from within and outside the EU/EEA between 2011 and 2017.

A long-term, year-on-year increase in reporting (Figure 1) can be observed which reflects the increasing number of CAPs authorised and is also attributed to the increased awareness of the value of pharmacovigilance reporting from veterinarians as well as a move to full implementation of the pharmacovigilance legislative requirements by the veterinary pharmaceutical industry. While there is still concern regarding underreporting, in particular for food-producing species, the increased dataset is a very positive development that enhances the ability to analyse the data effectively. There were noticeable increases in the number of reports in 2017 coming from Australia, Brazil, Croatia, Israel, Italy, Slovenia, South-Africa, Sweden, the United Kingdom (UK) and the United States.

The majority of reports concern companion animals, with adverse event reports in dogs and cats accounting for 90% of the cases. Further descriptive statistics regarding the reports received in 2017 can be found in Annex 1.

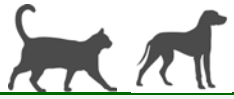
During 2017, the EMA CVMP and its PhVWP-V reviewed, in total, 155 PSURs provided by the MAHs. Further, the continued monitoring of centrally authorised VMPs through signal detection resulted in 561 surveillance reports based on potential signals of safety or lack of expected efficacy concerns. All signals detected were further analysed and, for some products, have led to the recommendation to add additional warnings to the product information or have led to a request to the MAH for a targeted PSUR (see tables below). For some signals the assessment concluded that the observed signs were either not likely to be associated with the use of the product or the observed signs fell within those adverse events expected following use of the product and/or were adequately addressed in the product information. A small number of analyses resulted in signals of potential safety or lack of expected efficacy concerns for which a potential causal relationship with the product administered could not yet be excluded. These issues remain under investigation in 2018 (see table below).

Also in 2017, EMA received a relatively high number of requests for information (39) and requests for data (88), the majority of which concerned potential safety issues related to anti-parasitic products in dogs and cats.

4. Findings and recommendations related to centrally authorised veterinary medicinal products

During 2017, the continued monitoring of signals and evaluation of PSURs resulted in the following findings and recommendations related to centrally authorised VMPs.

4.1. Companion animals



Activyl (indoxacarb)	A relatively high number of reports were noted that included neurological disorders (including deafness and blindness), allergic reactions, lethargy and anorexia in dogs and cats. The potential association between use of the product and these reported events continues to be monitored.
Activyl Tick Plus (indoxacarb/permethrin)	The MAH has been requested to monitor events that include sensitivity and neurotoxicity reactions potentially related to the use of the product and consider the need to update the product information. The MAH has also been requested to assess the impact of the change in the product information on the number of adverse event reports in cats and to further monitor adverse reactions in humans.
Advocate (imidacloprid/ moxidectin)	Due to the relatively high number of reports regarding convulsions, the MAH has been requested to monitor this signal for the next PSUR and consider updating the product information, if necessary.
Apoquel (oclaticinib)	Potential signals involving signs associated with respiratory tract disorders were identified during routine surveillance in 2017 and will continue to be monitored. Additionally, the MAH has been requested to continue monitoring reports involving unexpected signs associated with blood and lymphatic system disorders, in particular reports involving the signs lymphoma or lymphosarcoma and comment specifically on such reports in the next PSUR.
Bravecto (fluralaner)	The MAH provided a targeted PSUR that included an extensive analysis and review of all serious reaction reports with neurological disorders, skin and appendages disorders, hypersensitivity/immune mediated reactions and hepatopathy, including cases that led to death and/or death by euthanasia. After analysis of those data, the following changes to the product information were recommended (additions to text in **bold**): Section 4.5 Special precautions for use in animals **Use with caution in dogs with pre-existing epilepsy.** Section 4.6 Adverse reactions (frequency and seriousness) **Convulsions and** lethargy have been reported very rarely in spontaneous (pharmacovigilance) reports.

	In addition, as proposed by the MAH, a data capture aid has been made available to support veterinarians to record events that include neurological disorders, hepatopathy and death. Further surveillance of these events will be continued.
Broadline (fipronil, S-methoprene, epinomectin, praziquantel)	Monitoring of events that involve neurological signs and/or death will continue.
Canigen L4 / Nobivac (for active immunisation of dogs against *Leptospira*)	The MAH has been requested to provide a targeted PSUR on adverse events concerning death and/or death by euthanasia covering the period since authorisation until 31 December 2017.
Canigen L4, Nobivac L4 & Versican Plus DHPPi / L4, Plus DHPPi / L4R, Plus L4, Plus Pi / L4, Plus Pi L4R (for active immunisation of dogs against *Leptospira*)	A high number of reports of painful local reactions and systemic reactions were reported with different multivalent *Leptospira* vaccines. Further investigations on the underlying cause e.g. potential role of the additional antigenic load, are under investigation.
Cardalis (benazepril hydrochloride /spironolactone)	The MAH has been requested to provide a cumulative review of all adverse event reports involving coughing, focussing on those cases reporting a dry cough. The MAH has also been requested to closely review gastrointestinal and dermatological signs for the next PSUR.
Cytopoint (lokivetmab)	A potential signal involving blindness was detected during routine surveillance in 2017. Reports involving eye disorders, particularly blindness, will continue to be monitored.
Metacam (meloxicam)	Updates were recommended for section 4.9 of the SPC and accordingly section 8 of the Package Leaflet for the Metacam oral suspension for dogs (additions to text in **bold**, deletions in ~~strikethrough~~). It is recommended that a small measuring syringe is prepacked with the product, along with the large measuring syringe. 4.9 Amounts to be administered and administration route Oral use […] Dosing procedure using the measuring syringes: **The syringes fit onto the bottle and have a kg-body weight scale which corresponds to the** maintenance **dose (i.e. 0.1 mg meloxicam / kg body weight). For the first day, twice the maintenance volume will be required.** **The suspension could be administered using the small syringe for dogs less than 10 kg body weight (one graduation mark corresponding to 0.5 kg of body weight) or the large syringe for dogs over 10 kg body weight (one graduation mark corresponding**

	to 2.5 kg of body weight). ~~The syringe fits onto the drop dispenser of the bottle and has a kg body weight scale which corresponds to the maintenance dose. Thus for initiation of the therapy on the first day, twice the maintenance volume will be required.~~
Nexgard (afoxolaner)	The MAH provided a targeted PSUR on all neurological events reported since authorisation. The outcome of the analysis of the data resulted in a recommendation to amend the product information to include the following additional warning: **Neurological signs (convulsions, ataxia and muscle tremors) have been reported very rarely.**
Osurnia (terbinafine, florfenicol, betamethasone acetate)	The MAH has been requested to continue monitoring of eye disorders in animals following exposure to Osurnia and propose appropriate actions, as necessary.
Simparica (sarolaner)	The MAH has been requested to evaluate and comment on a possible association between Simparica administration and immune-mediated disease/reactions in the next PSUR.
Suprelorin (deslorelin acetate)	The MAH has been requested to further investigate the mechanism(s) underlying testosterone modulation of seizure susceptibility in dogs.
Trifexis (spinosad/milbemycin oxime)	The MAH will continue to monitor adverse event reports relating specifically to gastrointestinal and neurological effects.
Vectra Felis (pyriproxyfen / dinotefuran)	The MAH has been requested to continue the monitoring of adverse events involving application site disorders in cats.
Vectra 3D (dinotefuran, pyriproxyfen and permethrin)	The MAH has been requested to continue monitoring application site reactions, as well as reports of anxiety, behavioral disorders NOS, hyperactivity, vocalization, lethargy and anorexia.
Zycortal (desoxycortone)	The MAH has been requested to continue to monitor adverse events associated with electrolyte imbalance.

4.2. Food producing animals

Bovela (for active immunisation of cattle against bovine viral diarrhoea (BVD))	Following the assessment of the observed adverse events it was recommended to the MAH to amend the product information with the following text (additions to text in **bold**, deletions in ~~strikethrough~~): Section 4.4 Special warnings for each target species […] **A definitive diagnosis of persistent infection can only be established upon re-testing in blood after an interval of at least 3 weeks. In some limited cases with new born calves, positive ear notches for BVDV vaccine strain were reported by molecular diagnostic tests. Additional laboratory tests to differentiate vaccine strain virus from field strain are available.** […] Section 4.7 Use during pregnancy, lactation or lay While persistent infection of the foetus caused by the vaccine was not observed, transmission of vaccine virus to the foetus ~~cannot be ruled out~~ **may occur**. In addition the MAH was requested to: • provide information on the characteristics of "iatrogenic" persistently infected (PI) calves (e.g. whether the vaccine strain is found only in the skin, confirmation of the persistency of the infection including data on the investigation at a second time-point, the frequency of these events, details of the dam's vaccination schedule and specifically whether it was primo-vaccinated with Bovela) and on the epidemiological impact of these calves on the BVD control programmes undertaken throughout Europe; • encourage pharmacovigilance reporting to identify similar events of potentially "iatrogenic" PI calves and to ensure appropriate diagnostic investigations have been conducted; and • monitor and critically discuss reproductive disorders including abortion, return to oestrus, or similar clinical signs in relation to the overall benefit-risk balance of the product; In addition monitoring of allergic reactions and hypersensitivity reactions will be continued.
Eravac (for active immunisation against rabbit haemorrhagic disease type 2 virus)	Reports of lethargy and death will continue to be monitored.

Kexxtone (monensin)	A relatively high number of reports were noted that included regurgitation of the bolus, which could alter the efficacy of the product and could lead to accidental ingestion of the active ingredient by dogs, which could be lethal. Therefore, this issue will continue to be monitored even though at this point the recommendations included in the SPC are deemed appropriate.
Imrestor (pegbovigrastim)	Reports of dystocia, hypocalcaemic condition, ketosis, premature parturition, retained placenta, ruminant stomach disorder, stillbirth, mastitis and metritis will continue to be monitored.
Panacur AquaSol (fenbendazole)	Reports of death, lethargy, anorexia, egg drop, enteritis, hepatobiliary disorders and splenomegaly will continue to be monitored.
Suvaxyn PCV (for immunisation of pigs against Porcine Circovirus type 2 (PCV2))	The MAH was requested to undertake appropriate diagnostics for lack of expected efficacy events to identify the strains involved, as there have been reports of potentially new variants in the field. The MAH had also been requested to comment on the efficacy of the vaccine derived from the PCV2a genotype against the different PCV2 genotypes encountered in the field. This issue may also be applicable to other PCV-vaccines and is being considered for the respective products on a case by case basis.
Zolvix (monepantel)	The MAH is encouraged to continue monitoring lack of expected efficacy which could lead to the potential development of resistance and to discuss lack of expected efficacy in the next PSUR.

4.3. Humans

Activyl (indoxacarb)	Adverse reactions were reported in humans involving [application site] pruritus, eye irritation and erythema which will continue to be monitored.
Apoquel (oclaticinib)	A potential signal relating to immunosuppression in humans following repeated handling of the product was noted during routine surveillance in 2017. Future reports of adverse events in humans following dermal exposure will continue to be monitored to ensure that warnings in the product information remain adequate.
Bravecto spot-on (fluralaner)	A relatively high number of reports was received that included local skin reactions that occurred due to spillage during administration and/or close contact with the animal following administration. Users are strongly advised to use gloves during the administration as outlined in the product information.
Cerenia (maropitant citrate)	The MAH has implemented the following wording in the SPC: **People with known hypersensitivity to maropitant should administer the veterinary medicinal product with caution**. Human adverse events reported following exposure to the product will continue to be monitored.

Equisolon (prednisolone)	The MAH has agreed to add the following user safety warnings to the product information: **It is recommended to wear gloves and protective respiratory mask during handling and administration of the product**.
Osurnia (terbinafine, florfenicol, betamethasone acetate)	The MAH has been requested to continue monitoring eye disorders in animals and humans following exposure to Osurnia and propose appropriate actions as necessary.
Suvaxyn Circo+MH RTU (for active immunisation of pigs against porcine circovirus type 2 and *Mycoplasma hyopneumoniae*)	The MAH has been requested to continue to monitor reports of human adverse events and, as part of the next PSUR, to consider the need for adding recommendations on user safety (guidance on remedial action to be taken following accidental contact or a description of the expected outcome of a self-injection) to the SPC.
Improvac (induction of antibodies against gonadotropin-releasing factor (GnRF) conjugated to dipthheria toxoid)	The MAH has been requested to perform a thorough follow-up on human exposure cases investigating in particular the extent to which a recommended safety injector was used. Furthermore, the MAH has been requested to consider the need for new user safety warnings regarding persisting inflammatory injection site reactions after accidental injection in a finger or in or around a joint. In one report, amputation of a finger because of a severe injection site reaction was reported.
Upcard (torasemide)	The MAH was requested to follow-up events that include visual disorders and pancreatitis (which are expected adverse effects in humans) and were observed in the previous reporting period.

5. Findings and recommendations related to non-centrally authorised veterinary medicinal products

While pharmacovigilance of non-CAPs falls under the responsibility of each Member State there are regulatory tools within the EU that are established to allow early communication of safety concerns and rapid exchange of pharmacovigilance information between national competent authorities and EMA, such as the rapid alert (RA) and non-urgent information (NUI) communication exchange systems. Furthermore, in 2017, EVVet was used as a tool for monitoring adverse events of vaccines that are not authorised in the EU/EEA but which are used for control of emerging animal diseases. This will strengthen also the cooperation between EMA and the European Food Safety Authority (EFSA) with regard to the collection and analysis of adverse events during emergency vaccination campaigns.

The following non-centrally authorised veterinary medicinal products were discussed during 2017 at the level of the PhVWP-V:

Hipnoton 10 mg/ml solution for injection for horses and cattle (detomidine hydrochloride)

Starting in November 2016 an increase in the number of lack of expected efficacy events was reported for this product in the UK. In total 9 lack of expected efficacy reports were received relating to approximately 32 horses and involving two batches of product. In all cases, the veterinarians involved reported that higher doses than recommended were required to achieve the desired level of sedation, or they found the product was having no effect at all. The incidence estimate for lack of expected efficacy in horses based on the UK data was estimated to be 0.19%. This product has been on the UK market since 2011. These reports were considered unusual as no adverse events had been reported prior to this cluster of lack of expected efficacy reports.

A rapid alert was issued by the UK national competent authority. Both batches were recalled from the supply chain to the level of the veterinarian and distribution was suspended in the UK. Following investigations, the MAH identified that low temperature impacted on efficacy of the product and agreed to submit a variation to amend the product information to highlight the issue. The MAH will continue to analyse the stability of future batches.

Orniflox (enrofloxacin)

The product is authorised for administration to rabbits, small rodents, reptiles and avian species via gavage. The German national competent authority received 4 adverse event reports after administration of the product concerning gingival disorders, buccal necrosis and erosion in rabbits and a guinea pig that had to be euthanised. The adverse events occurred following oral administration of the product, rather than by gavage. No similar adverse events had been reported from other Member States after use of the product so the issue would be followed up at national level.

Flortek 100 mg/ml solución para administración en agua de bebida para porcino (florfenicol)

Since 2015 eight reports were received concerning neurological signs and deaths in pigs after the administration of Flortek solution for use in drinking water. After a review of other products containing florfenicol as active ingredient, two similar reports relating to other products with the same pharmaceutical form were identified. A similar report was also noted for an injectable product. To date there was no definitive conclusion on the underlying cause of the neurological signs and deaths. However, the marketing authorisation holder proposed to amend the product information to include these signs as potential adverse events.

Genta 100 mg/ml (gentamicin)

Discussions in 2017 continued on the rapid alerts initiated in 2016 relating to gentamicin containing products. The rapid alerts were originally circulated following receipt of adverse event reports concerning horses presenting with signs of anaphylactoid reactions such as urticaria, increased breathing frequency, colic-like signs, trembling and sweating. All adverse events were reported shortly after a new batch of the finished product produced with a new batch of the active pharmaceutical ingredient (API) gentamicin was placed on the market. Regulatory actions, including batch recalls and caution in-use communications, were taken in some Member States.

Early in 2017, the marketing authorisation holder for Genta 100 identified that the batches causing adverse events contained much more histamine than those for which no adverse events were reported. A correlation between the concentration of histamine and the occurrence of adverse events was found. The clinical signs reported were considered consistent with the pharmacological profile of histamine and there was also a correlation in time. It was noted that the manufacturer of the active pharmaceutical ingredient had taken measures to reduce the histamine content in the active substance in October 2017. Considerations are on-going at EU level on the need for determining a scientifically-justified limit for histamine in gentamicin medicinal products and on any further measures deemed necessary.

6. Overall conclusions

One fifth of all the reports contained in EVVet were submitted in 2017 which represents a significant increase in reporting to the database considering that it is operational since 2005. The increase can be attributed to a number of elements including:

- the provision of "non-serious" reports which are not legally required to be submitted but were provided for certain PSURs and/or were provided as part of a pilot exercise with volunteering industry partners;
- an increase of reports in dogs associated with the use of certain anti-parasitics which may have been influenced by media attention, including social media, in certain Member States; and
- a marked increase of reports due to maturation of pharmacovigilance systems in certain "third countries", in particular Australia, Brazil, Israel and South-Africa.

The entire pool of 253,000 reports within the EU central database and the improvement of analytical tools and expertise enable better monitoring and follow-up of the post-marketing pharmacovigilance data.

The CVMP agreed on several improvements to the product information for centrally authorised VMPs as a direct result of pharmacovigilance surveillance. For the majority of centrally authorised VMPs the adverse event reports were considered in line with the approved product information and the benefit-risk balance remained unchanged. For a small number of products, investigations are continuing to further validate the potential signals observed and corroborate with future data.

As a therapeutic group, the anti-parasitic products accounted for 40% of all reports in the database. This was followed by immunological products (vaccines) accounting for 23% of all reports (Figure 4). These figures correlate with the relative sales of such products and therefore do not necessarily mean that these groups of products are more hazardous than other product types.

The total number of reports involving food producing animals declined compared to 2016. It is concluded that the efforts up to now to try to address underreporting for food-producing animals has not had a significant effect to date although additional initiatives are planned for 2018 to establish direct interaction between regulators and specialised veterinarians of certain food producing species.

It is recognised that increased transparency and feedback are important factors for encouraging veterinarians to report adverse events and it is hoped that this bulletin provides information of value to the practitioner. Establishing a dynamic and active interaction with veterinarians who have the expertise on the use of VMPs in practice and regulators is essential for improving animal and public health. Therefore, all veterinarians in the EU are encouraged to report any adverse events, including potential lack of expected efficacy to the national competent authority in their country or to the relevant MAH of the product involved[5]. Several authorities have online templates to facilitate reporting. The continued increase of the number of reports in the central EU database, EVVet, is fundamental for improving adverse event surveillance and allows authorities to provide better feedback to the veterinarians on the safe and effective use of VMPs in the EU. For 2018 there will be continued focus to increase transparency and direct communication on pharmacovigilance related issues to veterinarians in the EU.

[5] Certain Member States require veterinarians to report directly to the national competent authority only.

Annex I
Descriptive analysis of adverse event reports received in EudraVigilance Veterinary

A total of 26,598 reports relating to exposure to centrally authorised VMPs were received in 2017. These include 25,890 adverse event reports relating to animals and 708 adverse event reports relating to humans exposed to VMPs.

The adverse event reports received concerned 152 products, which is approximately 80% of the total CAPs with a valid marketing authorisation granted by the end of 2017.

Of the 25,890 reports in animals, 23,225 reports concerned companion animals, most frequently dogs (19,540) and cats (3,685) and 2,665 reports concerned food-producing animals.

Of the reports received for CAPs in 2017 10,828 occurred in EU/EEA countries. The 15,761 reports originating from outside the EU/EEA were from the United States (68%), Brazil (12%) and Canada (9%) with the remainder being, listed in order of the number of reports received as follows: Australia, Japan, South Africa, New Zealand, Colombia, Switzerland, Mexico, Israel, Taiwan, China, Korea (South), Serbia, Argentina, Ecuador, Russia, Ukraine, Puerto Rico, Thailand, Honduras, Mozambique, Zimbabwe, Chile, Costa Rica, Lebanon , Philippines, Singapore, Turkey, Botswana , Peru, India, Malaysia and the Bahamas.

Table 1 and the figures in this annex show the numbers of reports by target animal species (in addition to humans). A single report may relate to one or more animals or individuals (especially for treatment concerning livestock) and to one or more products, which may have been used concurrently.

The table gives raw figures of reports received, irrespective of whether or not the reaction can be definitely attributed to administration of the product.

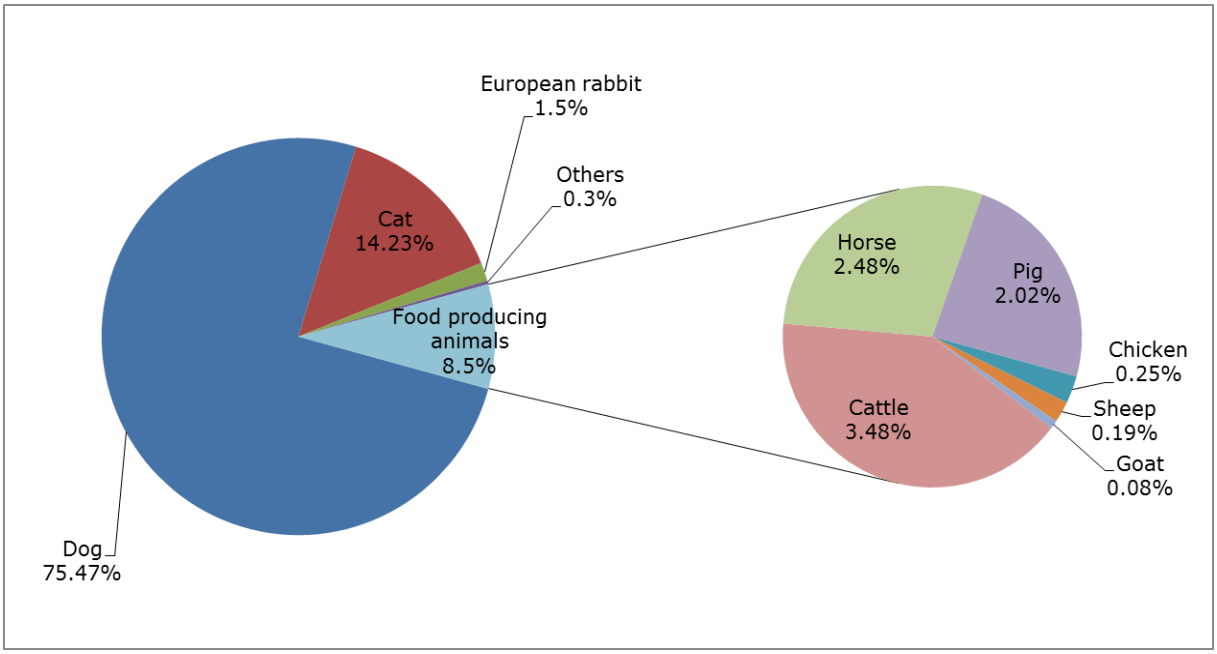


Figure 1. Proportion of adverse event reports by species received during 2017 following the use of centrally authorised products.

Summary statistics on reports for CAPs by target species, including reports in humans received between 1 January 2017 and 31 December 2017 are presented in the table below.

Table 1. Reports received between 1 January 2017 and 31 December 2017 for CAPs by target species, including reports in humans.

Animal reports	Species	Number of safety reports	Number of animals affected
Animal	Dogs	19,540	20,873
	Cats	3,685	4,518
	Cattle	902	17,428
	Horses	639	1,020
	Pigs	524	126,209
	Rabbits	387	608
	Other*	78	50,695
	Chicken	65	1,331,513
	Sheep	50	1,553
	Goats	20	4,373
Total animals		**25,890**	**1,558,790**

Human reports	Number of safety reports	Number of humans affected
Humans	708	708
Grand total	**25,598**	**1,559,498**

* “Other” species include mainly donkey, ferrets and guinea pigs amongst others.

The total number of animals reacting and safety reports within the EU central database by species until 2017 is presented in Figure 3 below. The logarithmic scale on the y-axis allows the inclusion of both the number of reports received and the total number of affected animals (which, in particular for food producing animals, can be a multiple of the actual number of reports).

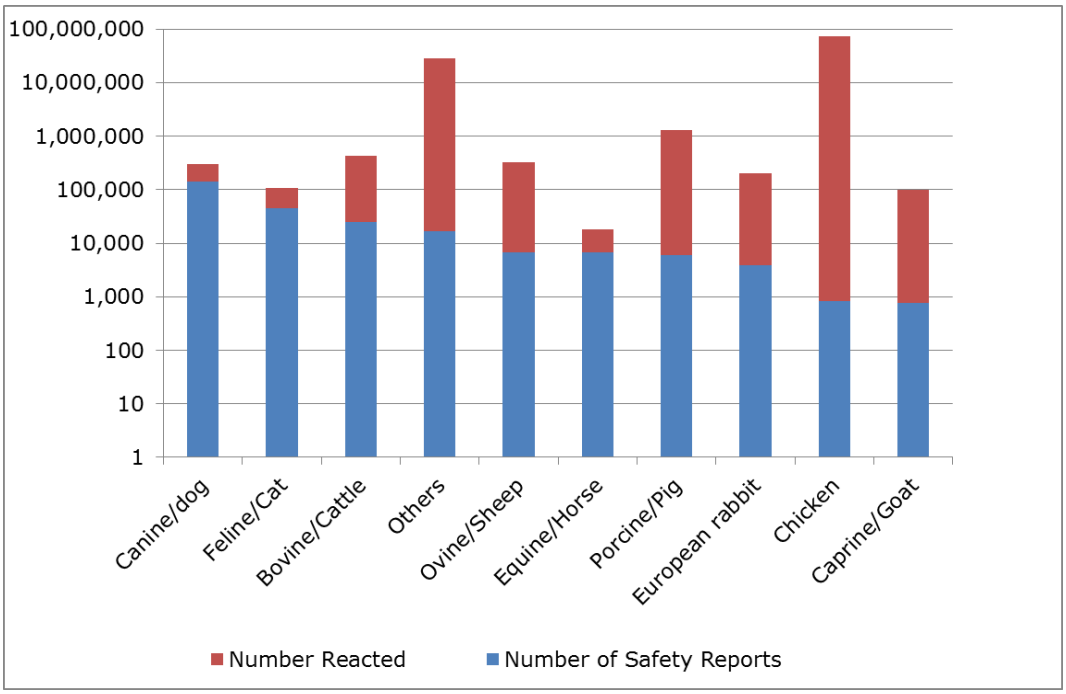


Figure 2. Total number of reports and animals affected by species in EVVet (1 January 2005-31 December 2017).

In the following Figure the reports of adverse events in various animal species and in humans for all products have been grouped according to the anatomical therapeutical chemical (ATCVet) coding system (see http://www.whocc.no/atcvet/ for further explanations). The number of adverse event reports classified by ATC coded type of product until 2017 is presented in the figure below.

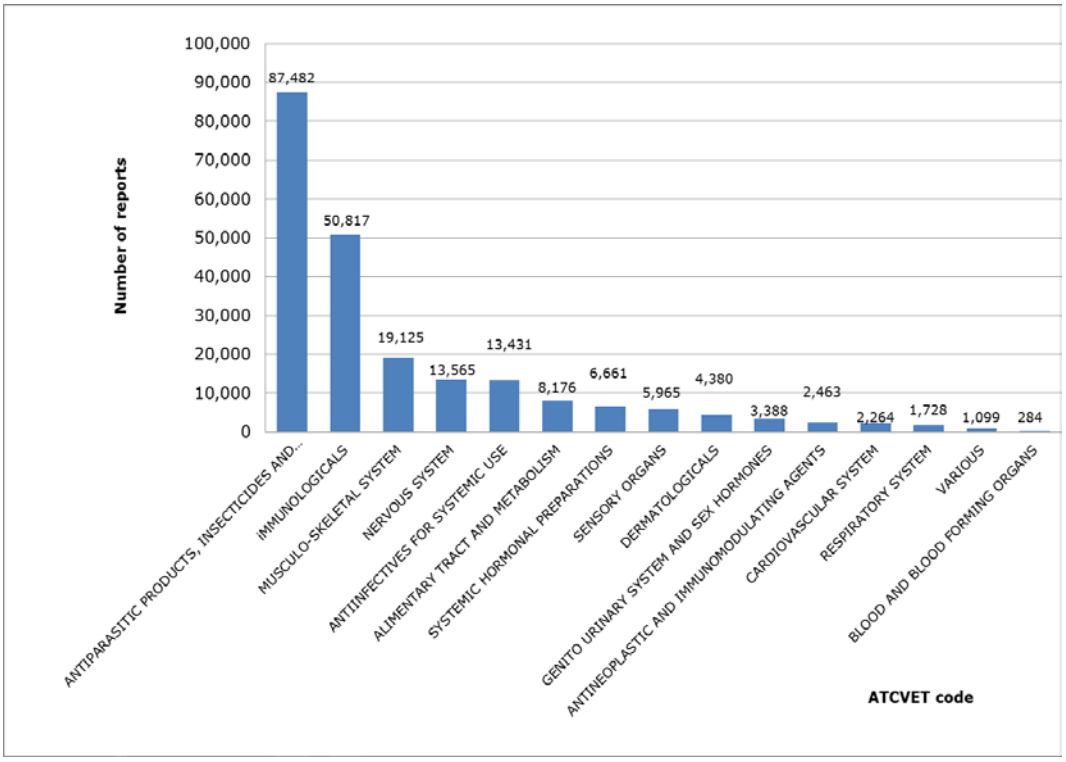


Figure 3. Total number of reports by ATCVet group in EVVet (1 January 2005-31 December 2017).