Outcomes of the online questionnaire on the quality of veterinary products and pharmacovigilance

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Regional Webinar for OIE National Focal Points for Veterinary Products
(6th Cycle) 17-19 February 2021 (Europe, English)

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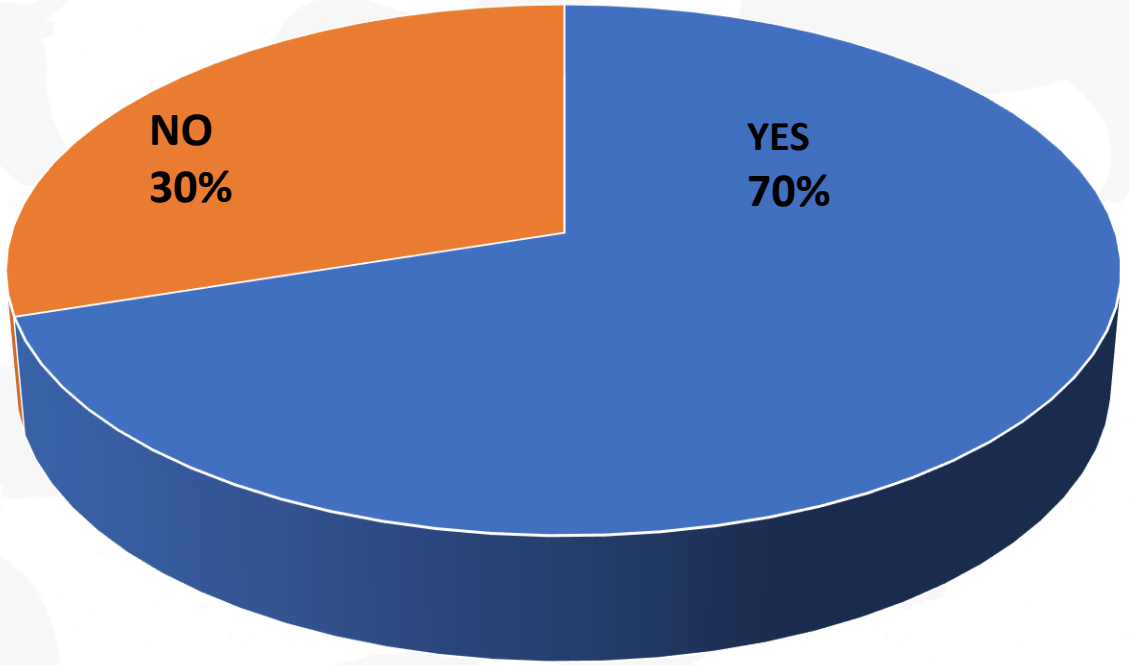
Country answer



Outcomes of the online questionnaire on the quality of veterinary products and pharmacovigilance

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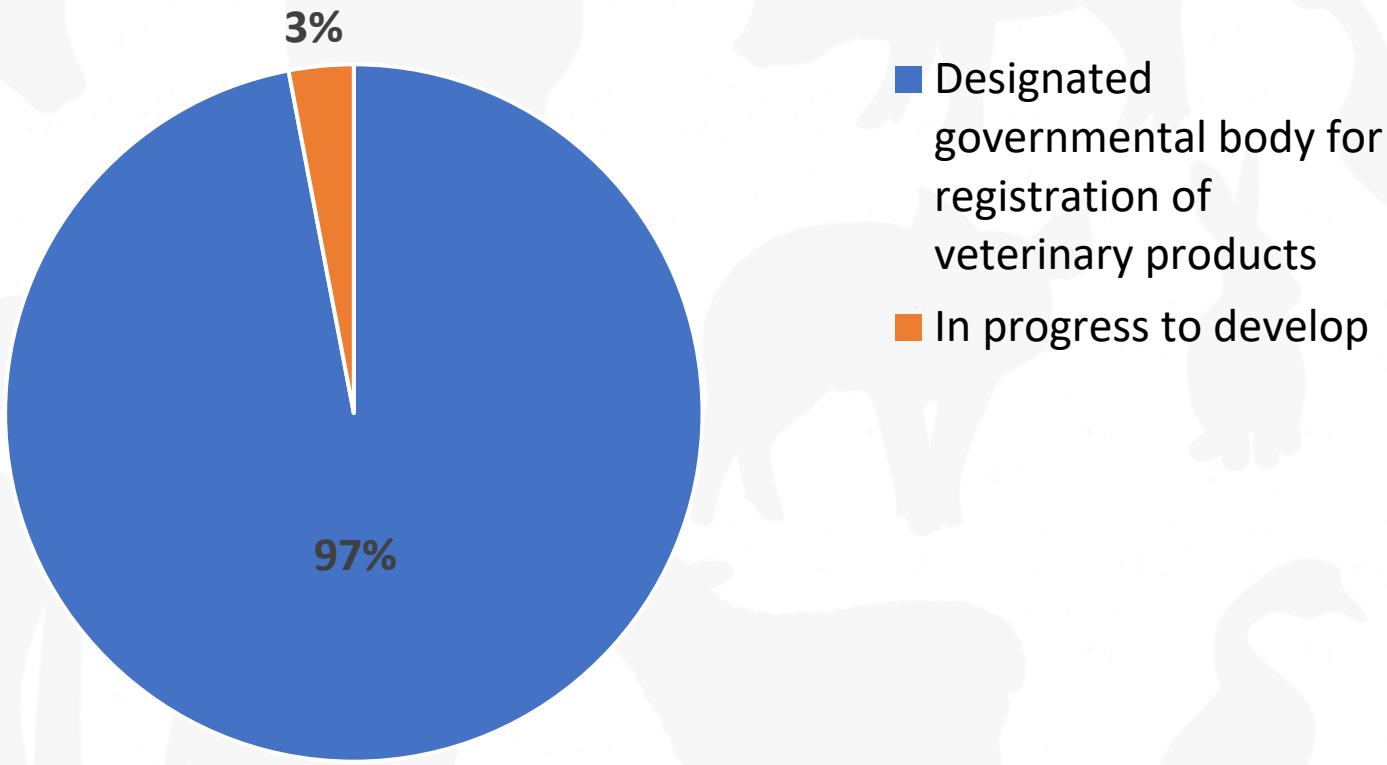
1. Does your country currently have a designated governmental body for registration of veterinary products, or is there work in progress to develop it?



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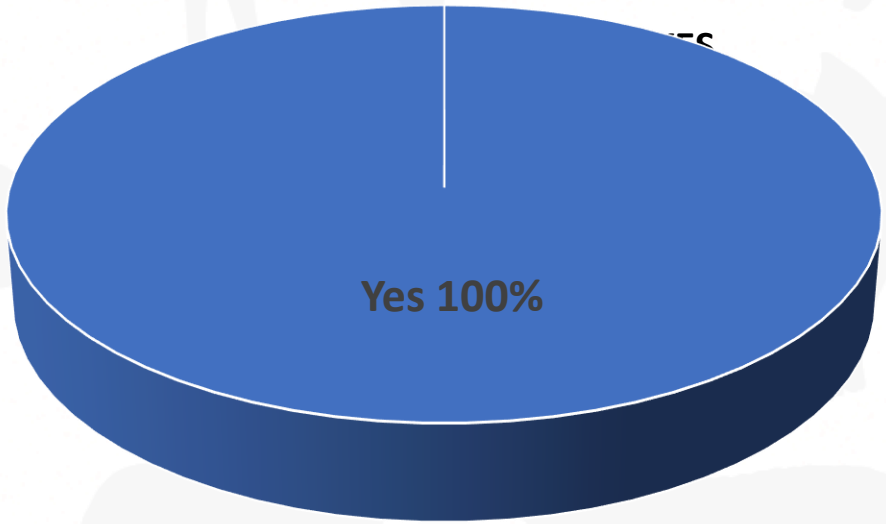
If you have designated governmental body for registration of veterinary products; do you have a database or list for all authorized/registered veterinary medicinal product



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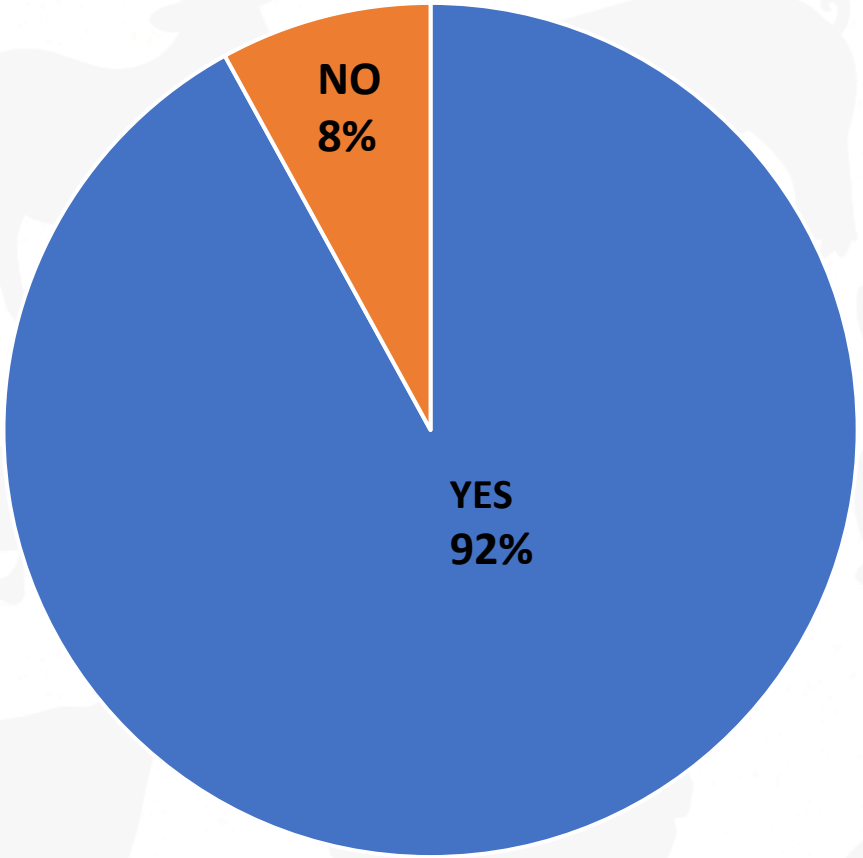
Is the list of registered products publicly accessible?



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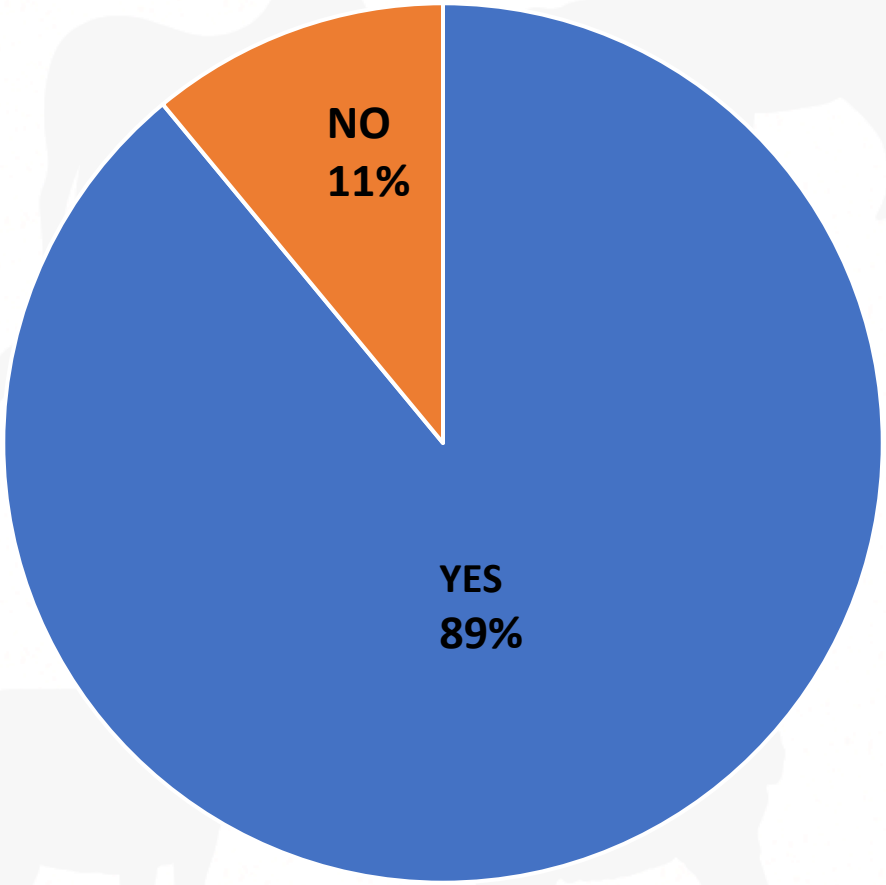
Do you have pharmacovigilance (PHV) legislation implemented in your country?



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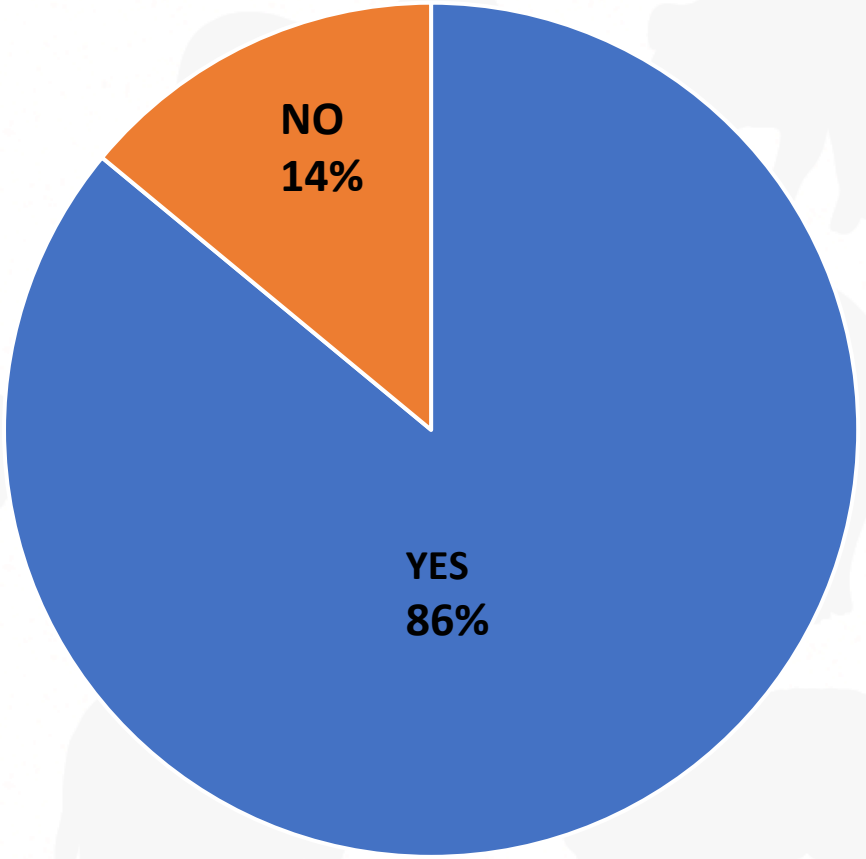
Do you have a functioning pharmacovigilance system in your country?



Outcomes of the online questionnaire on the quality of veterinary products and pharmacovigilance

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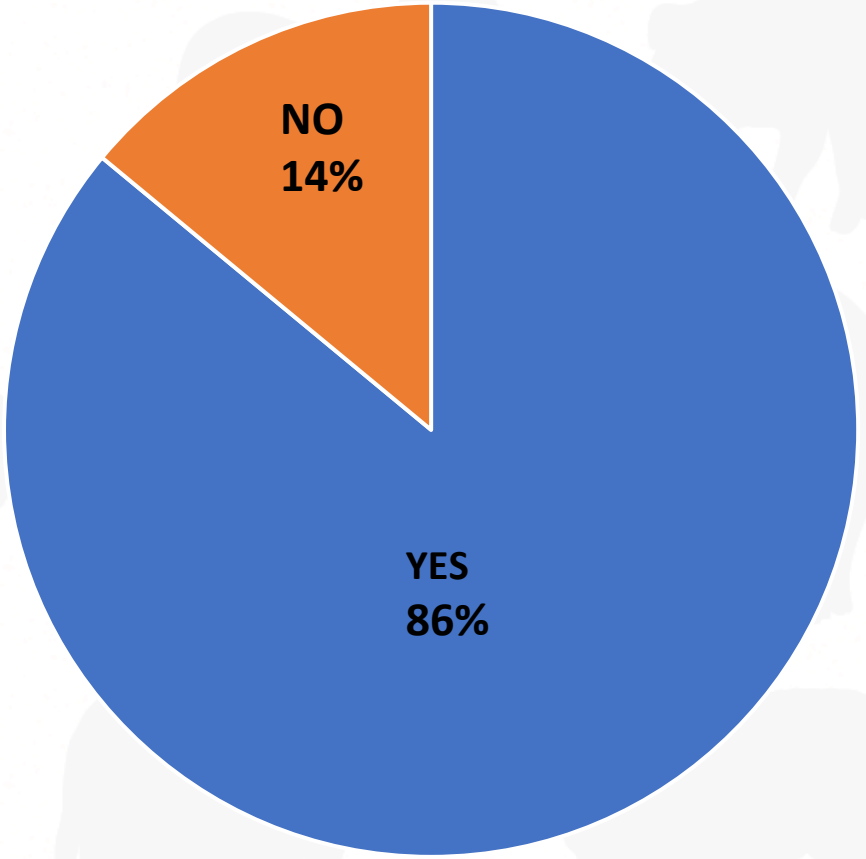
Do you have a PHV guideline(s) that are used in the post-marketing activities in your country?



If you have a pharmacovigilance system, please describe the key elements of the pharmacovigilance system

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- According to Directive 2001/82/EC marketing authorization holders are required to submit periodic safety update reports (PSURs) to the national competent authority (NCA), which is the Federal Office for Safety in Health Care (BASG). These reports (documentation and evaluation of all expected and unexpected adverse reactions, spontaneous reports from veterinarians, findings from clinical studies, observational studies, scientific literature, etc.) may indicate, for example, a lack of efficacy due to the development of resistance in the target parasites. A detailed benefit-risk assessment is performed and countermeasures in case of new (resistance) risks are initiated. If there is sufficient evidence of the lack of efficacy of an antiparasitic against a parasitic pathogen, this may result in the corresponding pathogen being removed from the indications for use or further warnings being included in the product information.
- Registration, data collection, quality control, signal detection, control for import, audit inspections, regulatory actions, capacity building
- Regional level: EU database for adverse events (AEs) and signal management, guidelines, pharmacovigilance working party. National level : three key elements can be identified: A quality system with standard operating procedures for pharmacovigilance, audits and training of pharmacovigilance staff. Recording and follow up of AEs: For this a national recording system (excel), an electronic reporting system for veterinarians, animals owners or other healthcare professionals and dedicated mailboxes for AE, PSURs and Rapid alerts exist. The AEs and Periodic safety Report (PSUR) are followed by pharmacovigilance experts. Communication: formation of students and/ or veterinarians on pharmacovigilance, communication through website or social media of the Agency, providing feedback on questions on pharmacovigilance

If you have a pharmacovigilance system, please describe the key elements of the pharmacovigilance system

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- The veterinarian is obliged to inform the Ministry, the manufacturer and the authorized representative about all new effects and undesirable consequences of the use of the medicine
- The access to the system is 24 hours per day on the internet pages available. We are directly connecting with Eudra Vigilance Veterinary base with EMA
- The veterinarian pharmacovigilance system consist of a national database to archive and track reported adverse events. Eudravigilance Veterinary database (EVVET) it is used
- ADR reporting system in place for vets and animal holders/owners, rapid alert system for quality issues
- The pharmacovigilance department is under the Ministry of Health. The Ministry of Health works in collaboration with the National Veterinary Services (IVS), which is under the Ministry of Agriculture and Rural Development, regarding all veterinary products. Registered drugs (veterinary and human) are first approved in a special committee formed by members and professionals from both ministers mentioned above. Registered drugs are publicly listed in the Ministry of Health website

If you have a pharmacovigilance system, please describe the key elements of the pharmacovigilance system

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- The pharmacovigilance system is the head of the Ministry of Health and consists of the Ministry itself and the Regional Pharmacovigilance Centres. The Ministry of Health promotes and coordinates, also in collaboration with the Institute health, studies and research on the use of the veterinary medicine products, the epidemiology and organises plans to take samples the from distribution circuit of the veterinary medicinal products already registered; The Ministry of Health adopts measures to promote spontaneous reports from healthcare professionals; maintains the necessary relations with the Agency, with the other Member States, with the international bodies: and with the regions and autonomous provinces. The regions and autonomous provinces can establish regional pharmacovigilance centres, using the regional veterinary institutes, University faculties of medicine veterinary or other specialized centres. The Ministry of Health can take emergency measures, suspend, revoke or modify the conditions of the MA in order to limit its indications or availability, change dosages or add a contraindication or warning.
- The pharmacovigilance team comprises of pharmacovigilance assessors (assessment of PSURs and reports) and pharmacovigilance inspectors. The EMA pharmacovigilance database, EVVET2, is used as database for all spontaneous pharmacovigilance reports.

If you have a pharmacovigilance system, please describe the key elements of the pharmacovigilance system

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- During veterinary pharmacovigilance, information is collected for the monitoring of veterinary medicinal products and attention is paid to adverse reactions. The information obtained shall be scientifically evaluated to ensure that appropriate and harmonized decisions are taken on veterinary medicinal products. According to the requirements for registration, production and supply of veterinary medicinal products to the market, legal entities holding veterinary pharmacy licenses, veterinarians engaged in veterinary activities or veterinary pharmaceutical companies and other health care professionals must notify the SFVS of suspected serious adverse reactions or unexpected adverse animal and human adverse reactions

- The pharmacovigilance system is based on collect of Adverse Event Reports from veterinarians, other health professionals like pharmacist, veterinary nurses and also from aninal owners. We have a special email address to receive the reports. We also can receive the reports from Marketing Authorisation Holder (MAH). We assess the reports and classify the relation between each veterinary medicinal product (VMP) or human product according to ABON classification. On 2022 we will adopt the classification defined on new European Rule (NVR). After the assessment, we introduce the case on EudraVigilance Veterinary (EV Vet) database and send it to European Medicines Agency (EMA) mailbox within this database, and also to MAH mailbox also on EV Vet.

If you have a pharmacovigilance system, please describe the key elements of the pharmacovigilance system

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Known adverse reactions of a VMP are listed in the Summary of Product Characteristics (SPC) and in the package leaflet, documents prepared for each authorized VMP. Users (veterinarians, owners) report suspected adverse reactions to the competent authority – National Sanitary Veterinary and Food Safety Authority / Institute for Control of Biological Products and Veterinary Medicines or to the distribution network (retail or wholesale) or to the marketing authorization holder of the concerned VMP. The leaflets remind users to discuss the suspected side effects with veterinarians. Adverse reactions are usually reported by veterinarians prescribing or administering the veterinary medicinal product, but animal owners are also able to report suspected adverse reactions directly to the competent authorities by e-mail or to the marketing authorization holders through the reporting forms. The adverse reaction reporting form is available on the competent authority site. Adverse reaction reports are used to evaluate the benefits and risks of the VMPs during product development and to monitor its safety post authorization. The type of action depends on the nature, severity and frequency of the adverse reaction, as well as the intended use of the VMP, the benefits of its use in relation to the risks and the existence of alternative therapies.

In the case of confirmation by scientific assessment of a problem with a VMP or active substance, possible regulatory measures may include the following:

- conducting post-authorization studies in order to obtain additional information on the safety profile of the VMP or active substance;
- performing a complete re-evaluation of the benefit-risk profile of the VMP or active substance;
- changing the information about the VMP (for example, adding contraindications, warnings, precautions or additional information about side effects);
- modification of the packaging in order to clearly mention the risks and instructions for VMP use;
- transmission of information to veterinarians / users regarding risks (through letters, warnings, publications or specialized websites);
- adding warnings in leaflets;
- issuing safety releases, such as press releases;
- suspension of the marketing authorization;
- withdrawal of the VMP from the market..

If you have a pharmacovigilance system, please describe the key elements of the pharmacovigilance system

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Veterinary pharmacovigilance is the set of actions of territorial control suitable for verify that the distribution, dispensing and use of the medication take place correctly to protect the health of consumers of food of origin

Control the use of veterinary medicines in animals, pursue the "black and gray" market for veterinary drugs.

Key elements:

Logging of all drug passages throughout the distribution chain.

The timely, rapid and effective detection of news fundamental for a residue research plan.

Monitoring of treated animal species.

Monitoring of the most used molecules.

To find distributional anomalies.

Monitoring of the quantities of medicines prescribed.

The analysis of suspension times.

If you have a pharmacovigilance system, please describe the key elements of the pharmacovigilance system

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- a) During authorisation of VMPs

- Evaluation of Detailed Description of the Pharmacovigilance System by competent authority in the field of VMPs; Qualified person for pharmacovigilance has to be appointed.

b) After authorisation of VMPs

- The obligation of the MAHs of VMPs to record, report to the competent authority and evaluate of AEs has been introduced
- Possibility for vets and animal owners to report the suspected AEs to competent authority has been introduced
- Evaluation of reported spontaneous AEs and Periodic Safety Update Reports by competent authority and adoption of appropriate measures, if necessary (e.g. suspension of the distribution, withdrawal of the product from the market product, suspension of registration, change of Summary of Product Characteristics etc.) and sharing the information with CAs of other MSs (EVVET). If necessary testing is performed by own Official Medicines Control Laboratory
- Inspection of PHV system of MAHs should be performed by competent authority (currently not performed)

c) Other

- The obligation for the veterinary sponsor to report serious adverse reactions, unexpected serious adverse reactions recorded by investigator during the clinical trial of VMP has been introduced
- Evaluation of reported AEs by competent authority from the clinical trial and adoption of appropriate measures, if necessary (e.g. suspension or cancellation of a clinical trial)

- A PHV system is in place for more than 20 years. It designed the PHV system and the obligations of the healthcare professionals and marketing authorization holders (specially all aspects related to the notification of all the suspected adverse events due to the administration of a veterinary medicinal product) and the obligations of the regional administration (basically to promote PHV and participate in the corresponding technical) and central administration (Medicines and Medical Devices Agency –AEMPS-). AEMPS is assisted by two permanent technical committees (Veterinary Medicines Safety Committee and national Technical Pharmacovigilance System Committee.)

If you have a pharmacovigilance system, please describe the key elements of the pharmacovigilance system

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- PV System is based on VICH and EMA guidelines and recommendations. Reports are collected and evaluated. Periodic Safety Update Report reporting is based on International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products and EMA recommendations. Adaptation to new veterinary EU regulation is ongoing.

- All new veterinary products, before being imported, undergo an official registration procedure, after receiving registration, a permit for import and sale is issued, the state body for the supervision of veterinary products constantly monitors official veterinary pharmacies to prevent the sale of counterfeits and other unregistered veterinary products

- All spontaneous adverse event reports are recorded in the national database and in Eudravigilance Vet (EVVet), in accordance with timelines specified in EU legislation. Periodic safety update reports, signal management and other phv tasks are handled in accordance with EU legislation / guidelines

If you have a pharmacovigilance system, please describe the key elements of the pharmacovigilance system

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- The PV system is based on voluntary reporting of adverse event by owners and veterinary professionals. They can choose to report directly to the marketing authorisation holders or to VMD, the regulator. They can submit reports via an online reporting form available on our website or via a paper form. Marketing authorisation holders have a legal requirement to submit all adverse event reports to VMD. All adverse events are entered into a database which includes quality and validation controls to ensure quality data entry; and it includes statistical analysis tools to analyse the data to detect signals of concern for products. We also require marketing authorisation holders to submit periodic safety update reports for each product they have an authorisation for. These are submitted at intervals set in legislation. This report should include sales information and an overview of the benefit risk balance of the product. All data is collated and analysed, action is taken depending on findings – such as requiring the marketing authorisation holder to make changes to their product label, or in some cases suspending an authorisation. We also conduct inspections of marketing authorisation holders to ensure they have an appropriate pharmacovigilance system in place and are following all requirements set in the legislation.

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If you have a pharmacovigilance system, please describe the key elements of the pharmacovigilance system

The pharmacovigilance system is in place designed to monitor the safety of authorised medicinal products and detect changes to their risk-benefit balance.

The State Agency of Medicines:

- informs persons qualified to prescribe medicinal products, pharmacists, assistant pharmacists and the public of the need to report the adverse reactions of medicinal products;
- accepts information about adverse reactions in a web environment and on paper and take appropriate measures to obtain accurate and verifiable data about adverse reactions, in order to assess the information scientifically;
- collects and assesses pharmacovigilance data to determine whether there are new risks, whether risks have changed or whether there are changes to the risk-benefit balance of a medicinal product;
- takes the appropriate measures for prevention and reduction of risks relating to pharmacovigilance;
- informs persons qualified to prescribe medicinal products, pharmacists, assistant pharmacists and the public of the emergence of risks relating to the use of medicinal products;
-(mainly human medicines) assesses the results of the risk minimisation measures specified in the risk management plan drawn up by a marketing authorisation holder and the results of the measures specified in the conditions of the marketing authorisation;
- (mainly human medicines) assesses the updating of the risk management system;
- inspects the functionality of the pharmacovigilance systems of marketing authorisation holders and their compliance with the requirements of quality systems, provided that the pharmacovigilance system master file of the pharmacovigilance system is located, and participate in inspections organised by other Member States;
- once every two years, carries out an audit of the pharmacovigilance system and submits to the European Commission a report on the audit results (applies to human medicines);
- participates in the joint work-sharing of the Coordination Group and Pharmacovigilance Risk Assessment Committee of the European Medicines Agency and pursue relevant cooperation with the competent authorities of other Member States;
- at the request of the European Committee, participates in the international harmonisation and standardisation of the technical measures of pharmacovigilance, which is coordinated by the European Medicines Agency;
- follows the recommendations of the Coordination Group and Pharmacovigilance Risk Assessment Committee of the European Medicines Agency upon implementation of risk minimisation measures and decisions of the European Committee regarding the measures to be applied due to marketing authorisations granted in the Member States.
- The State Agency of Medicines must inform the European Medicines Agency, the competent authorities of other Member States and the marketing authorisation holder of newly identified risks, changed risks or a change to the risk-benefit balance of a medicinal product.
- The State Agency of Medicines updates the assessment report where new information important from the point of view of assessment of the quality, safety or effectiveness of a medicinal product is obtained.

If you have a pharmacovigilance system, please describe the key elements of the pharmacovigilance system

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The treating **veterinarian is obliged to notify** to the central competent authority (CCA) any adverse reactions observed on animals or on humans ascribed to the use of a certain veterinary product.

The CCA collects, analyses and forwards the information to the **database** (Eudravigilance system).

Marketing authorisation holders (MA holders) are obliged to have permanently and continuously an appropriately **qualified person** responsible for pharmacovigilance and shall maintain detailed records of all suspected adverse reactions, including all suspected serious adverse reactions and human adverse reactions relating to the use of veterinary medicinal products that are brought to his attention, and report them promptly to the competent authority, including those in a third country.

MA holders also have to send a regular **safety report** to the CCA on the collected pharmacovigilance data. The periodic safety update reports shall include a scientific evaluation of the risk-benefit balance of the veterinary medicinal product.

The CCA – based on the evaluation of the pharmacovigilance reports – can suspend or withdraw the marketing authorisation of a certain product or modifies the leaflet accordingly.

If you have a pharmacovigilance system, please describe the key elements of the pharmacovigilance system

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Pharmacovigilance is performed by a national competent authority for the authorisation of veterinary medicinal products and postmarketing surveillance, the Federal Office for Consumer Protection and Food Safety (BVL). The key elements are the detection, assessment, understanding and prevention of suspected adverse events or any other problem related to a veterinary medicinal product and taking appropriate measures to ensure a positive benefit risk balance. There is an own national database for the collection, assessment and submission of adverse events. The pharmacovigilance system is integrated in the quality management system of the BVL.

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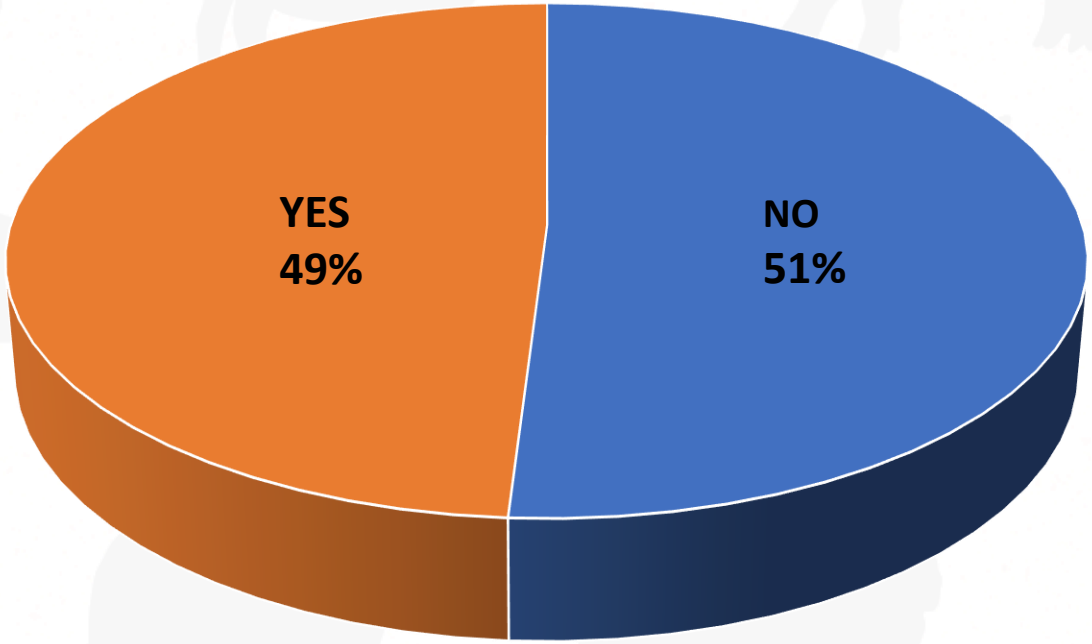
What role(s), if any, do you think the OIE should play in defining the minimum requirements for a pharmacovigilance system for veterinary medicinal products?

Coordination among different stakeholders in order to avoid too many disharmonized systems to be developed worldwide



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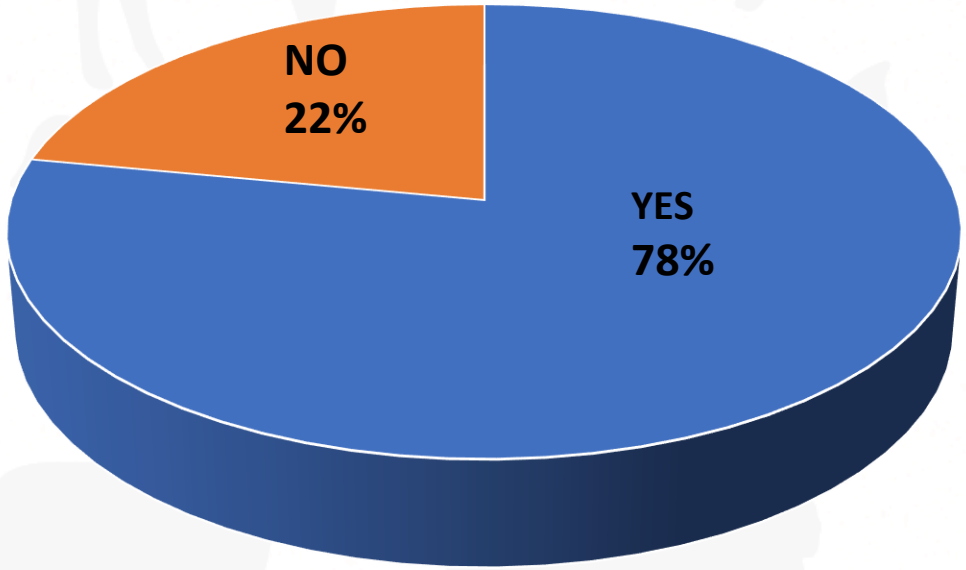
What role(s), if any, do you think the OIE should play in defining the minimum requirements for a pharmacovigilance system for veterinary medicinal products?

Prepare a chapter in the OIE Manual or Code on the minimum requirements how to set up a basic pharmacovigilance system to provide standard/guideline(s) for the OIE Member Countries



Outcomes of the online questionnaire on the quality of veterinary products and pharmacovigilance

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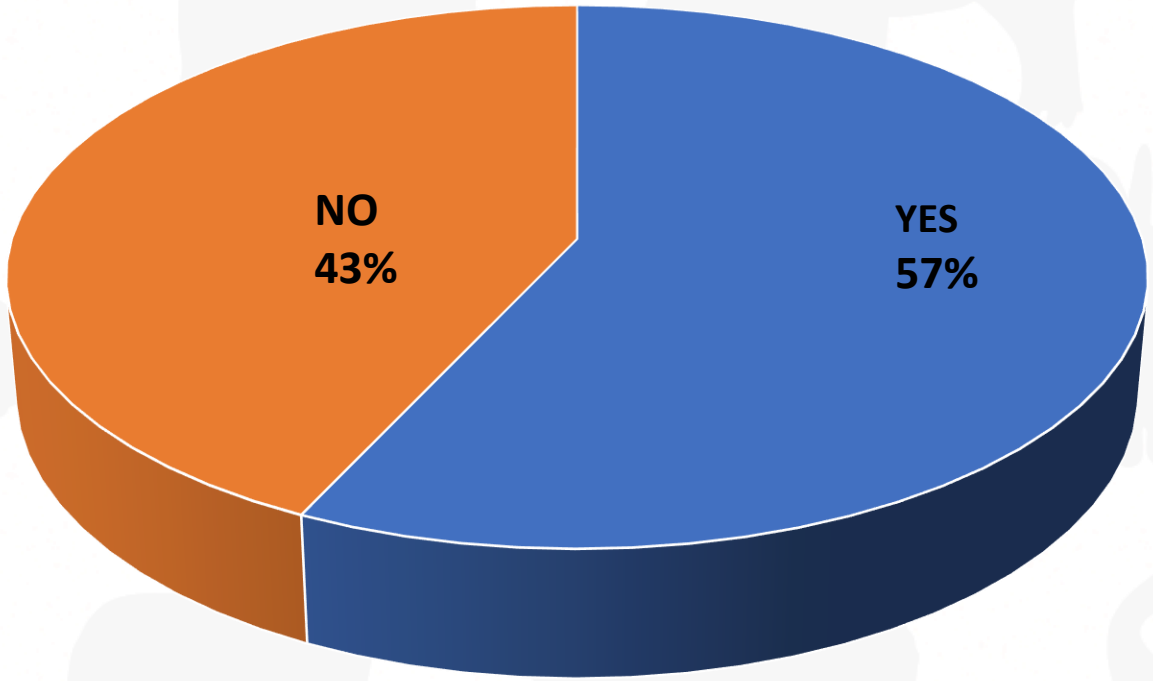
Do you think that an OIE document describing how to set up a basic pharmacovigilance system would be beneficial for your country?



Outcomes of the online questionnaire on the quality of veterinary products and pharmacovigilance

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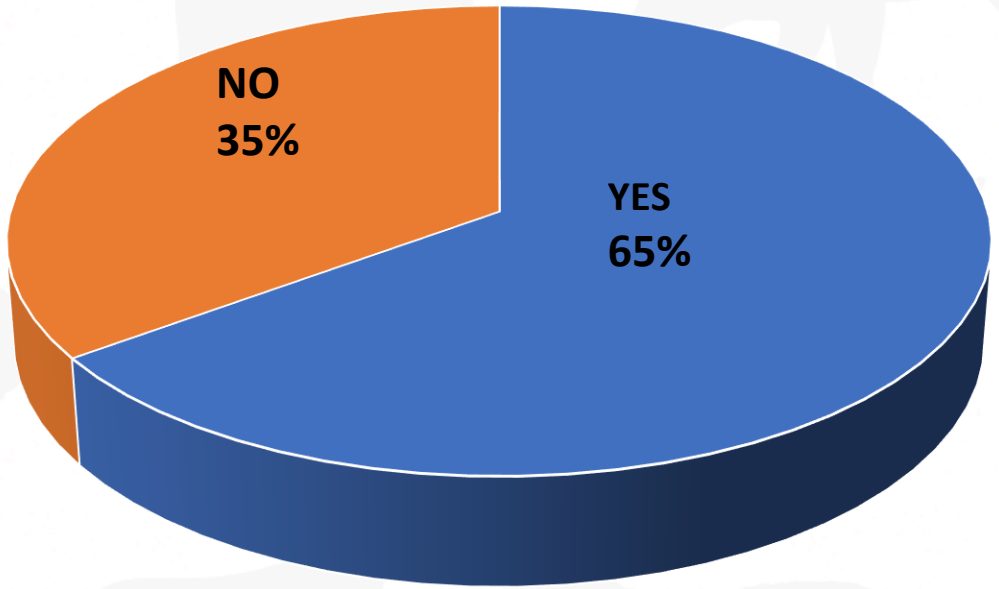
Do you consider that a pharmacovigilance system could be set up at a Regional -Sub-Regional level?



Further thoughts, comments or proposals

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Do you consider that a pharmacovigilance system could be set up at a Regional -Sub-Regional level?

- If the number of pharmacovigilance data justifies such a request. However, management of pharmacovigilance system must be centralized in order not to lose information.
- Especially for smaller countries this should be useful
- It depends on the definition “regional, sub-regional”. If that means international, definitely yes. If it means regions of the same country, probably not.
- EU has a regional pharmacovigilance network, which demonstrates this approach is viable. Having regional pharmacovigilance systems in place is hugely beneficial as signal detection is reliant on a certain volume of data and therefore sharing data provides a benefit to all. However, it is very difficult to maintain due to the requirement for consistency in the coding and entry of data to ensure that the data can be used appropriately for analysis.
- At EU level, pharmacovigilance is already operating at regional level for centralized authorised products. This provides the possibility to have a bigger pool of information and in this way detecting more quickly specific issues. The input of different countries in the discussion of specific issues also contributes to a better overview/ understanding and a harmonised way of handling pharmacovigilance

Further thoughts, comments or proposals

Do you think that an OIE document describing how to set up a basic pharmacovigilance system would be beneficial for your country?

- Veterinary pharmacovigilance system which is in place under EMA, which is well established and in many ways comparable to human pharmacovigilance systems; furthermore, with the soon-to-come implementation of the new veterinary drug legislation (EU regulation 2019/6), the EudraVigilance Veterinary (EVV) pharmacovigilance system is being improved even further. Therefore, we do not believe that descriptions of basic pharmacovigilance systems would be of direct value for our agency. However, we warmly encourage OIE activities in this regard, to improve veterinary pharmacovigilance globally, which would indirectly certainly also benefit our agency, as part of the pharmacovigilance data which we receives and reviews under the EEV system is from non-EU countries
- Even if there is an advanced pharmacovigilance system established, additional guidance documents could be helpful since every system can be further developed.
- We would like to propose that VICH (International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products) requirements be extended to all the World