

# GOOD VETERINARY PHARMACOVIGILANCE PRACTICE GUIDE



# Foreword

**This IFAH-Europe<sup>1</sup> Good Veterinary Pharmacovigilance Practice Guide is a very good illustration of the animal health industry initiatives to promote veterinary pharmacovigilance and it is a great pleasure to see its second edition coming off the press.**

The first edition, launched in March 2004, was elaborated following a joint workshop with competent authorities and veterinarians (FVE<sup>2</sup>) in May 2002. Veterinary pharmacovigilance has since come a long way and IFAH-Europe undertook this revision to reflect the changes to the regulatory environment. While most sections of the GVPPG have been updated to a certain extent, the main changes relate to the addition of the following new references: Detailed Description of the Pharmacovigilance System; the initiative on Periodic Safety Update Reports synchronisation and work-sharing; electronic reporting and pharmacovigilance inspection.

Thus, this Good Practice Guide provides a useful tool for anyone in industry involved in veterinary pharmacovigilance. It should be read in conjunction with the legal texts, but does not bind industry or the relevant authorities or any other party involved.

Finally, I wish to express special thanks to the IFAH-Europe Pharmacovigilance Working Party for its contribution to the release of this 2<sup>nd</sup> edition and the European competent authorities who responded positively to this industry initiative.

Brussels, April 2011



**Sylvie Meillerai**  
Technical Project Manager  
IFAH-Europe

<sup>1</sup> IFAH-Europe International Federation for Animal Health - Europe <http://www.ifaheurope.org/>

<sup>2</sup> FVE Federation of Veterinarians of Europe <http://www.fve.org/>

## About IFAH-Europe

IFAH-Europe (International Federation for Animal Health-Europe) is the federation representing manufacturers of veterinary medicines, vaccines and other animal health products in Europe. It represents both corporate members and national animal health associations in Europe. These associations comprise both local, small and medium-sized enterprises (SMEs) and international companies. IFAH-Europe's membership covers 90% of the European market for veterinary products.

## Mission

IFAH-Europe's mission is to promote a predictable, harmonised, science-based marketplace for the provision of innovative, quality, animal health products that contribute to the supply of safe, healthy food and to high standard of health and welfare for animals and people.

As a responsible industry, we want to ensure that our stakeholders understand the work we do and the broad range of benefits we provide for society at large. To achieve this, as the voice of the European animal health industry, we encourage constructive dialogue with governments, public policy makers, legislators, regulators, non-governmental organisations, the veterinary profession, the food chain, consumers and other stakeholders.





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# 1 INTRODUCTION: THE IMPORTANCE OF GOOD PHARMACOVIGILANCE PRACTICE

**Pharmacovigilance is the systematic collection, collation and analysis of reports from veterinarians, pharmacists and animal owners, of adverse reactions or events connected to the use of a veterinary medicinal product.** Its purpose is to identify unwanted properties in relation to substances and products that could not be observed in the development process since testing during development is always limited to a relatively small number of individuals compared to the real world. In that respect it is just another phase in the life of a medicinal product. This post-authorisation surveillance also includes reactions in humans, lack of expected efficacy, off-label use, violation of maximum residue limits and potential effects on the environment.

Pharmacovigilance was first addressed in the legislation in Directive 81/851/EC when Marketing Authorisations were renewed every 5 years. More recently, Directive 2001/82/EC as amended by Directive 2004/28 and Regulation 726/2004, replaced the 5-yearly renewal with a single administrative one, to apply to both new and existing products. The post-marketing surveillance system was consequently strengthened and the reliance on large amounts of pre-registration data reduced to move towards a more targeted and potentially higher level of product assurance.

With pharmacovigilance now being a very essential part of the regulatory process, it is the responsibility of all interested parties (i.e. animal owners, veterinarians, the animal health

industry and the competent authorities) to work together to ensure that it is implemented fully and consistently in all member states and within all companies.

**The purpose of this good practice guide is to provide a useful tool for the animal health industry to apply a consistent pharmacovigilance system in line with the legislative requirements.** Companies are fully aware of the need to accurately monitor suspected adverse events, to collect and evaluate the information to be reported to the authorities, and take appropriate measures if needed. This guide makes pharmacovigilance easy by answering the “what, when and how” questions. Above all, this guide demonstrates that the animal health industry is fully dedicated to running an efficient and fully operating pharmacovigilance system and is a reliable link in the reporting chain.

The animal health industry is also actively participating in the ongoing VICH process, which aims at harmonising technical requirements for veterinary product registration between the EU, US and Japan. The more homogeneously pharmacovigilance is performed, the more valuable will be the results.



# THE EUROPEAN PHARMACOVIGILANCE FRAMEWORK

## 2.1 WHAT IS THE RIGHT TERMINOLOGY FOR SUSPECTED ADVERSE REACTIONS?

Directives, Regulations, guidelines and communications from authorities use different terminologies to describe a pharmacovigilance (PhV) case. The most common denominations are:

- Adverse Drug Reaction;
- Suspected Adverse Reaction;
- Suspected Adverse Drug Reaction;
- Adverse Event.

The term 'Adverse Event' (AE) is used throughout this guide, since it is most often the case in documents prepared by Competent Authorities (CAs) and in VICH guidelines.

## 2.2 WHERE CAN THE RELEVANT LEGAL TEXTS BE FOUND?

Pharmacovigilance obligations are described in Directive 2001/82, as amended by Directive 2004/28, Regulation 726/2004 and in the Eudralex Volume 9B<sup>1</sup>. The links to the legal texts and other official documents are given in Appendix 1.

## 2.3 WHAT ARE THE LEGAL OBLIGATIONS OF AN ANIMAL HEALTH COMPANY?

1. Each company must include in every Marketing Authorisation Application a Detailed Description of its PhV System (DDPS) (Part IA - Ad-

ministrative data [5.20] of the dossier). Any change to your system that is described in the DDPS must be notified to the CAs according to Commission Regulation 1234/2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products. You should also refer to the Guideline on the details of the various categories of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products, where all changes to an existing DDPS are classified as Type IA 'Do and Tell' (see section C.I.9 of the guideline).

2. Each company must have a Qualified Person for PhV (QPPV) responsible for a system to collect and collate all the information about any adverse events that are reported to the personnel of the company, including sales representatives. The QP must reside in the Community and the system must be accessible at least at one point within the Community (see section 4.1 to find out more about the QPPV).

3. All companies must make sure to report:

- Serious animal cases and human adverse events within 15 days and electronically except under exceptional circumstances.
- All other adverse events in the periodic safety update reports (see section 3.4).

4. Every company must ensure that any request, from the Competent Authorities (CAs) of any of the Member States (MSs) of

<sup>1</sup> Publication of final Volume 9B was pending at the time the GVPPG went to print; in the meantime, Volume 9 (June 2004) remains valid for veterinary medicinal products

the EU for the provision of additional information necessary for the evaluation of the benefits and risks afforded by a Veterinary Medicinal Product (VMP) is answered fully and promptly. This includes the provision of information about the volume of sales or prescriptions of the veterinary medicinal product concerned.

## 2.4 WHO ARE THE DIFFERENT STAKEHOLDERS IN VETERINARY PHARMACOVIGILANCE?

Pharmacovigilance involves several key stakeholders. The legal references clearly state the responsibilities of CAs, in establishing an efficient pharmacovigilance system, and Marketing Authorisation Holders' (MAHs) Qualified Person for PhV in collecting the data on AEs. All the relevant information is shared between the CA and the MAH, so they can fulfil their obligations and responsibilities, e.g. measures to be taken in relation to the use of a product. However, the whole system depends on the users (veterinarians, pharmacists and animal owners) of medicines fulfilling their ethical responsibility of reporting adverse events.

- The **reporter** of the adverse event plays a major role in the chain, ensuring the relevant information reaches the CAs and the MAHs. It is the role of the veterinarian, the pharmacist or the animal owner, to report any adverse events following administration of a veterinary medicinal product to an animal.
- The **Qualified Person for PhV** (QPPV) is the key industry person. By collecting all relevant data, he/she is the main reference for all pharmacovigilance information within his/her company. He/She also informs the authorities, and provides them with any additional information they might require (see section 4.1).
- The **national and European Competent Authorities** (CAs), i.e. the authorities of the EU Member States

and of Norway, Iceland and Liechtenstein and the EMA (European Medicines Agency), are engaged in evaluating the reports received from the field in light of the data available on the concerned product. They are also responsible for reviewing the benefit/risk analysis and, if need be, for taking appropriate management measures. They also provide guidance and, under the revised legal framework, have the right to conduct PhV inspections of MAHs PhV systems.

When sharing information, confidentiality must be ensured and industry fully respects any legal obligation in that respect. Besides this, we should keep in mind the primary purpose of pharmacovigilance, i.e. to guarantee public and animal health, and that in any decision we take, the public interest prevails.

## 2.5 WHAT IS THE GEOGRAPHICAL AREA IN WHICH EU PHARMACOVIGILANCE RULES APPLY?

Pharmacovigilance rules prevail in the whole European Economic Area (EEA). The EEA is composed of the EU 27 MSs plus Liechtenstein, Iceland and Norway. So, if you read EU in European pharmacovigilance rules, you should in fact read EEA.

## 2.6 IS THERE A FLOW CHART OR DECISION TREE AVAILABLE THAT REFLECTS THE REPORTING OF AEs IN VETERINARY PHARMACOVIGILANCE?

A generic decision tree on the recording and reporting of AEs in veterinary medicines in Europe can be found in Appendix 2.





# 3 PHARMACOVIGILANCE CASES

## 3.1 ADVERSE EVENT: DEFINITION, SCOPE AND NEED TO REPORT

### 3.1.1 Definition

#### 3.1.1.1 What is an adverse event?

An adverse [reaction] event is defined in Article 1 of Directive 2001/82/EC, as amended by Directive 2004/28/EC, as follows: “a reaction to a veterinary medicinal product which is harmful and unintended and which occurs at doses normally used in animals for the prophylaxis, diagnosis or treatment of disease or to restore, correct or modify a physiological function.”

#### 3.1.1.2 Is the scope of veterinary pharmacovigilance limited to reporting of AEs?

The scope of veterinary pharmacovigilance as defined in Article 73 of Directive 2001/82/EC, as amended by Directive 2004/28/EC, covers not only the reporting of AEs in animals, but also other aspects of post-authorisation surveillance as follows:

- Lack of expected efficacy of a veterinary medicinal product for the registered indications,
- Off-label use: adverse observations linked to any use not according to the Summary of Product Characteristics (SPC) including misuse and abuse of the product. So positive experiences after ‘off-label use’ do NOT need reporting from a PhV perspective,

- Reported violations of approved residue limits, possibly leading to investigations of the validity of the withdrawal period,
- Human exposure,
- Potential environmental problems.

#### 3.1.1.3 Does the use of the wording ‘adverse events’ imply that only reactions for which the company considers there is a possible causality link need to be reported to the Competent Authority?

No, all AEs that are processed must be reported, provided all minimum 4 criteria are met (see 3.1.1.4). This includes those reactions for which the company proposes a causality assessment code N or unlikely (see section 3.2 for further explanation on causality coding).

#### 3.1.1.4 What are the minimum data components that make an observation/report an AE report?

The report does not become an adverse event report until all following 4 criteria are met:

1. The source must be identifiable (e.g. veterinarian, pharmacist, animal owner) and should include the name and address of the reporter, if possible;
2. The animals/human beings involved must be identified:
  - Animal: species (minimum requirement); desired additional information: sex, age, weight and number of animals treated;
  - Human: name (or identity code), sex, age or child/adult;

3. Details of the product used: names of the product (the name of the molecule/active ingredient is not enough) and of the MAH;
4. Details of the reaction: you need to have a good idea of what has happened. A clinical report should be provided whenever possible.

For residue violation and environmental cases, you should refer to 3.1.2.9 and 3.1.2.10 respectively.

#### **3.1.1.5 Are there different types of AEs (apart from the scope)?**

An adverse event can be expected or unexpected on one hand (see section 3.1.1.6) and serious or non-serious on the other hand (see section 3.1.1.7). The legal definitions for these can be found in Article 1 (12) and (13) of Directive 2001/82/EC, as amended by Directive 2004/28/EC.

#### **3.1.1.6 What are 'unexpected' and 'expected' AEs?**

An unexpected AE is defined as a reaction that is not consistent with those described in the SPC. Conversely, an expected AE describes an observation that is already mentioned in the SPC. The expectedness has implications for AEs reported from a so-called third country, i.e. outside the EEA (see section 3.3).

#### **3.1.1.7 What is a 'serious AE'?**

In animals, any AE which results in death, is life-threatening, results in significant disability or incapacity, results in a congenital anomaly/birth defect or in permanent or prolonged signs in the animals treated is considered to be a 'serious AE'.

#### **3.1.1.8 How is the word 'serious' interpreted for each type of animal?**

In veterinary medicine, the existence of a variety of animal species and husbandry conditions requires a modified approach to the classification of a 'serious AE'. For example, in intensive animal production of species such as poultry, fish or bees, a baseline level of mortality rate is considered as 'normal' or 'expected'. These species are usually treated as a group and only an increased mortality rate, or severe signs, or variations of animal production levels exceeding the rates normally expected should be considered as a 'serious AE'.

However, in species like dogs, cats or horses, a single death constitutes a 'serious AE'. This also applies to cases of individual deaths in cattle, sheep, pigs, goats and rabbits even if they are kept in herds or flocks in intensive animal production because treatment is often performed on the individual animal and therefore a single death or severe signs have to be considered on an individual basis.

So, remember that for any animal kept individually, a single death constitutes a 'serious AE', whatever the species.

#### **3.1.1.9 Is every unintended and harmful observation after an off-label use of the product reportable as an AE?**

Yes, such observations must be reported as AEs.

#### **3.1.1.10 Are bad in-vitro sensitivity data to be reported as AEs?**

Not as such. A reported lack of sensitivity or a perceived rise in resistance is not an AE to a treatment. However, when MIC or sensitivity testing is carried out during the investigation of a report on a suspected lack of expected efficacy of an antimicrobial, the results should be included in the report of the investigation.

#### 3.1.1.11 Must an event be product-related to be called an AE?

The definition of an AE does not relate to the actual cause of the event and no connection between the case and a treatment is mentioned. The fact that the case is reported as happening within a reasonable time after treatment or exposure to the product is enough.

So, in practical terms, an AE is any harmful and unintended observation occurring in an animal or a human being after treatment with or exposure to a veterinary medicinal product (VMP). This rule aims to ensure that infrequent AEs are also detected.

#### 3.1.1.12 Are quality defects to be reported as AEs?

The EU definition of an AE does not cover quality defects and quality complaints, which are dealt with under GMP (see GMP Directive 91/412). These are therefore outside the scope of European pharmacovigilance if not accompanied by observations that would be consistent with the definition of an AE. However, multinational companies having the same product licensed in the USA will need to record those quality issues for their US colleagues.

#### 3.1.1.13 Are asymptomatic human exposures reported to the company considered as AEs?

Human asymptomatic exposures are not AEs, as they do not fulfil the four criteria (see 3.1.1.4). They are only exposures and not reactions. However, it is good practice that you record and file them and ensure a suitable follow up of such reports with the reporter.

### 3.1.2 Investigation and reporting of a reported AE by a company

#### 3.1.2.1 What are the basics a company needs to do when receiving an AE report?

Basically, a MAH needs to ensure that the event is:

- Recorded,
- Investigated,
- Reported and
- Causality assessed (section 3.2).

#### 3.1.2.2 Do all AEs need to be RECORDED?

Yes, all events need to be entered in the pharmacovigilance system, which your company is obliged to have (see 2.3). It is also recommended to keep records of those reports that do not meet the four minimal data components (see 3.1.1.4). It will enable you to demonstrate, in a transparent manner, the way these reports have been handled.

#### 3.1.2.3 Do all AEs need to be REPORTED?

Yes, but how and when you report differs depending on the seriousness of the event and on the region where it took place. An overview of the reporting requirements is presented in the 'decision tree' in Appendix 2.

#### 3.1.2.4 What is the general rule on reporting?

The general rule is that you need to report all AEs in the Periodic Safety Update Reports (PSURs) that must be presented as follows (see also section 3.4):

- Every 6 months after authorisation until placing on the market;
- Every 6 months during the first 2 years following initial placing on the market;

- Once a year for the following 2 years, then
- At three-yearly intervals.

Exceptions to the above reporting rule occur for:

- Serious animal AEs and human cases occurring in the EEA and brought to your attention or which you may have knowledge of must be reported electronically within 15 days to the MS(s) where the cases occurred (see 3.1.2.5 and 3.1.2.6).
- Serious unexpected AEs, human cases and any suspected transmission via an infectious agent<sup>2</sup> occurring in a third country, must be reported electronically within 15 days to the EMA database (see section 3.3 on third country reporting).

More detailed information can also be found in the reporting decision tree in Appendix 2.

### **3.1.2.5 Is the date by which the four minimal data components are met important for an AE report?**

Yes, the date of receipt of the minimum information by the MAH or any other party working on its behalf becomes day zero. From that day, your company QPPV has a maximum of 15 days to notify the relevant CAs of a serious case. However, it is recommended to notify the authorities as soon as you have the details of the reaction.

### **3.1.2.6 How should serious AEs be dealt with in general?**

You basically follow the same rules as for all AEs. You can refer to the decision tree in Appendix 2 to see what needs to be done. The major difference is that serious cases are to be reported within 15 days after day zero. That means 15 days starting on the day the four minimum criteria are known by the first person who receives the report in your European or national organisation.

### **3.1.2.7 Do all AEs need investigating?**

Your company needs to ensure that adequate information is gathered to be able to assess the reaction reported. The company must assess the seriousness, expectedness and causality code of a case (see section 3.2 on causality coding and 'ABON' system).

### **3.1.2.8 Do serious AEs need much closer investigation?**

MAHs are expected to fully validate and follow-up all serious AEs that have been reported. It is essential for MAHs to provide as complete data set as possible, including all relevant clinical information in order to facilitate the assessment. The original words used by the reporter should be provided even if they are subsequently classified or coded according to the MAH or the competent authority accepted terminology.

### **3.1.2.9 Are reports concerning the validity of the withdrawal period (residues above the MRL) to be reported as serious AEs?**

Where investigation of drug residues in tissues or products of treated animals casts doubt on the validity of the withdrawal period of a VMP, it is important that this information is brought to the attention of the CA responsible for the authorisation of the product. Such cases should be reported as an AE in the PSUR (see section 3.4).

### **3.1.2.10 How should reports on environmental cases be handled?**

For such cases, you should gather the following minimum information:

- The location,
- The animal involved,
- The nature of the suspected environmental problem and
- The suspected product(s).

<sup>2</sup> Meaning 'non-intended' infectious agents and only infectious agents shown to be present in the product, i.e. excluding those transmitted by poor administration technique, such as dirty needles...

Such reports are normally addressed in the relevant PSUR. However, in certain specific circumstances and in order to limit further environmental damage, such cases may need reporting to the relevant CAs in an expedited manner.

**3.1.2.11 How should mortality in a Suspected Lack of Expected Efficacy (SLEE) case be handled?**

Mortality is typically reported as a serious AE, including in case of lack of expected efficacy.

**3.1.2.12 What about AEs following the use of a veterinary premix?**

AEs occurring on or after treatment with an in-feed medication are reportable under the pharmacovigilance scheme. In fact, when medicated premixes, which have been incorporated in the finished medicated feed, are suspected of causing a reaction in animals or humans, both the premix and the medicated feed should be investigated without delay.

**3.1.2.13 What about reporting AEs for generic, copy cat and co-distributed products?**

‘Generic product’ is a commonly used terminology for products whose Marketing Authorisation (MA) derives from a registration previously granted to another comparable product. For a detailed definition, we advise you to refer to Article 13.1(a) of Directive 2001/82/EC, as amended by Directive 2004/28/EC. For the purpose of this guide we will limit the discussion to the following types and descriptions:

- True generic: a MA obtained via an abridged procedure as described in Article 13.1(a)iii of Directive 2001/82/EC, as amended by Directive 2004/28/EC.

- Informed consent (or copy cat): a MA obtained via an abridged procedure as described in Article 13.1(a)i of Directive 2001/82/EC as amended by Directive 2004/28/EC.
- Co-distribution: a product sold by two different companies under the same MA.

Type of MA	Company responsible	Specific instructions
True generic:	Each MAH is responsible for his own product.	Authorities will co-ordinate any action deemed necessary.
Informed consent (or copy cat): 1 <sup>st</sup> scenario:	The company holds both MAs and is therefore responsible for both products.	Any regulatory action will apply to both products.
2 <sup>nd</sup> scenario:	One MA is transferred; then each MAH is responsible for his own product.	Both MAHs must maintain close liaison and inform each other on reported cases. Any regulatory action will apply to both products.
Co-distribution:	The MAH is responsible.	The co-distributor must report the cases IMMEDIATELY to the MAH. The MAH will report to the authorities and will coordinate any further action.

### 3.1.2.14 Do AEs that have already been reported directly to the authorities (e.g. by a veterinarian or animal owner) need to also be reported by the company?

If the MAH is aware that another person has already reported a reaction to one of its products directly to the authority of a MS, the MAH should still report that same reaction, informing the authority that his report is likely to be a duplicate of a previous one.

In such a situation, it is essential the MAH provides all the available details, including any reference number provided to the reporter by the authority, in order to help identifying the duplicate.

### 3.1.2.15 Do all clinical signs need to be coded according to the VeDDRA codes and terms?

Yes, and you should refer to the latest version of VeDDRA available from the European Medicines Agency website<sup>3</sup> for the latest list of terms.

## 3.2 CAUSALITY CODING

### 3.2.1 What is causality coding?

MAHs should comment on whether they consider there is a causal association between the suspect product(s) and reactions(s) reported and should provide the criteria on which they have made the assessment.

### 3.2.2 How is this causality association expressed?

It is important that causality is expressed using the ABON system. For that purpose, the EMA/CVMP has developed a guideline, which

provides common understanding and uniform approach to performing causality assessment (see the relevant EMA/CVMP GL<sup>4</sup>).

According to this system, four categories of causality can be made:

A: probable.

B: possible.

O: unclassifiable, for cases where reliable data are not available or insufficient information is available to draw any conclusion; for such cases, you may also categorise as follows: O1: inconclusive (other factors prevent a conclusion but product association cannot be discounted).

N: unlikely to be product related.

### 3.2.3 What factors should be taken into account when assessing the causality of an AE?

In assessing causality, the following factors should be taken into account:

1. Associative connection in time, including de-challenge and re-challenge following repeated administration (in clinical history), or in anatomic sites.
2. Pharmacological explanation, blood levels, previous knowledge of the drug.
3. Presence of characteristic clinical or pathological phenomena.
4. Exclusion of other causes.
5. Completeness and reliability of the data in the case reports.
6. Quantitative measurement of the degree of contribution of a drug to the development of a reaction (dose-effect relationship).

### 3.2.4 What is the minimum basis to consider a case to be 'probable'?

For inclusion in category 'A' (probable), it is recommended that all the following minimum criteria be met:

<sup>3</sup> EMA website at: <http://www.ema.europa.eu/htms/vet/phvwp/eudravigilance.htm>

<sup>4</sup> EMA/CVMP GL on Harmonising the approach to Causality Assessment for adverse reactions to VMPs (EMA/CVMP/552/03-Final): [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Scientific\\_guideline/2009/10/WC500004995.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/10/WC500004995.pdf)

- There should be a reasonable association in time between the administration of the drug and onset and duration of the reported case.
- The description of the clinical phenomena should be consistent, or at least plausible, with the known pharmacology and toxicology of the drug.
- There should be no other equally plausible explanation(s) of the case (if such are suggested: are they validated? What is their degree of certainty?).

The concurrent use of other drugs or the presence of disease should be taken into account in the assessment. If either of these could possibly be responsible for the signs, this makes it impossible to define the case as 'probable'.

Where any of the above criteria cannot be satisfied (due to conflicting data or lack of information), then such reports can only be classified as 'B' (possible), 'N' (unlikely) or 'O' (unclassifiable/not assessable).

Where re-challenge is undertaken, a positive re-challenge is a strong indication. A negative re-challenge makes it likely that the case should be category 'N'.

### **3.2.5 What is the minimum basis to consider a case to be 'possible'?**

Inclusion in category 'B' (possible) is recommended when drug causality is one (of other) possible and plausible causes for the described case, but when the data do not meet the criteria for inclusion in category 'A'.

### **3.2.6 What is the minimum basis to consider a case to be 'unclassifiable/not assessable'?**

For inclusion in category 'O', reliable data concerning an AE is unavailable or is insufficient to make an assessment of causality (O1: inconclusive).

### **3.2.7 What is the minimum basis to consider a case to be 'unlikely'?**

For inclusion in category 'N' (unlikely), sufficient information should exist to establish beyond reasonable doubt that drug causality was not likely to be the cause of the case.

### **3.2.8 Must human cases be coded?**

No, there is no obligation to code human cases.

### **3.2.9 In a case of concurrent use must other companies' products be coded?**

No, and it would probably be impossible since you have no access to the terms under which such a product was registered. The best way to address this concurrent use and to provide your opinion is in the assessment and/or narrative part, if appropriate.

### 3.3 THIRD COUNTRY REPORTING

#### 3.3.1 What is a third country?

A third country is a country outside the European Economic Area (EEA).

#### 3.3.2 Must an AE occurring in a third country be reported?

The legislation provides for serious unexpected AEs and human cases, as well as any suspected transmission, via a VMP, of any infectious agents<sup>5</sup> occurring in a third country to be made available to the Agency and the competent authority of the MS in which the product is authorised within 15 days. You are thus encouraged to report third country cases directly to the EMA database for these to be available to all authorities concerned.

A general overview on the reporting of AEs for third country reporting is included in the decision tree in Appendix 2.

#### 3.3.3 Are all AEs occurring in third countries reportable?

Broadly speaking yes. However, authorities allow, for practical reasons, some filtering in the reports to be submitted.

In VICH, it has been agreed that expedited submission to CAs in other VICH regions and observer countries, will occur when:

- An AE is an expedited submission in the country where the event occurs and
- The same VMP is approved in other VICH regions/observer countries and
- The animal species involved in the AE is a species approved in the other VICH regions/observer countries or
- There are serious implications regarding human safety.

In VICH, the same pharmaceutical VMP is defined as originating from the same MAH responsible for pharmacovigilance of this VMP with the same formulations, while the same biological VMP is defined as originating from the same MAH responsible for pharmacovigilance of this VMP with the same manufacturing specifications.

The most crucial information in addressing third country cases is whether the CAs of these countries deem necessary to take any regulatory action as a result of the reported cases.

#### 3.3.4 Who must these third country cases be reported to?

Serious unexpected AEs reports from third countries must be available to the Agency and the competent authority of the MS in which the product is authorised within 15 days. You are thus encouraged to report these cases directly to the EMA database so that they become available to all authorities concerned. In addition, all AEs from third countries should be reported in the line listing of the PSUR (see 3.4.2).

It has further been agreed at VICH that the PSUR should contain AEs for the same and similar pharmaceutical VMP(s) or same biological VMP (see 3.3.3 for definitions of 'same'). A 'similar pharmaceutical' VMP is defined as:

- Originating from the same MAH being responsible for pharmacovigilance of this/these VMP(s),
- The same active ingredients,
- Major excipients with the same or similar pharmaceutical function,
- At least one common registered species.

<sup>5</sup> Meaning 'non-intended' infectious agents and only infectious agents shown to be present in the product, i.e. excluding those transmitted by poor administration technique, such as dirty needles...



## 3.4 PERIODIC SAFETY UPDATE REPORTS (PSURs)

### 3.4.1 What is a PSUR?

A Periodic Safety Update Report is a product-specific document evaluating the safety of the product in practical use. It is produced at set times by the MAH for a veterinary medicinal product. It is intended to provide the competent authorities with an update of the worldwide safety experience of a VMP at set intervals post-authorisation. At these times, MAHs are expected to provide succinct summary information together with a critical evaluation of the benefit-risk balance of the product in light of any new or changing post-authorisation information.

### 3.4.2 What is the purpose of the PSUR?

The reporting of specific AEs aims to gather information on new or unknown cases, or to evaluate whether any direct action is required. PSURs, on the other hand, serve a different purpose, i.e. to evaluate whether new data have become available or whether the incidence of known effects has increased. This data could lead to further investigations, which might in exceptional cases lead to a change in the registered use of the product. In most cases, the analysis will confirm that the product is indeed safe and 'fit for use'. It is important to keep this purpose in mind when analysing these reports.

In addition to a line listing (see 3.4.5), the PSUR should classify the cases according to the ABON system. Most importantly, it should contain a critical evaluation of the benefit-risk balance of the product and put the observed cases in the right perspective, without being a lengthy narrative. It also gives the opportunity to outline if something, which has happened in field conditions, can explain certain changes in occurrence of cases. It should further

indicate whether further investigations and/or changes to the SPC wording are needed.

### 3.4.3 When must a PSUR be submitted?

Unless specified otherwise in your registration, PSURs should be sent as follows:

- Every 6 months after authorisation until placing on the market
- Every 6 months during the first 2 years following initial placing on the market
- Once a year for the following 2 years
- Then at three-yearly intervals.

The above schedule applies to all types of registrations. This timeline is quite obvious for nationally and centrally registered products. For decentralised procedures (MRP/DCP), the timeline is generally agreed upfront with the Reference Member State (RMS).

Also, authorities can request an additional PSUR in specific circumstances.

Furthermore, in 2007, the Heads of Medicines Agencies (HMA) launched an initiative for 'PSUR synchronisation and work-sharing'. Under this scheme, the PSUR submission calendars are synchronised per active substance. Where your product contains an active for which a harmonised DLP exists, you are encouraged to follow this calendar. This scheme also provides for the synchronisation of PSURs for vaccines over 6 months periods. You should refer to the HMA website for details of this initiative: <http://www.hma.eu/236.html> where you will find the necessary references including a 'Questions & Answers' document; you may also contact your national CA for further details.

### 3.4.4 What data must be included in the PSUR?

In order to carry out a good assessment, the report should not only contain data on the AEs, but also include the following:

- A copy of the latest approved SPC, unless you submit a PSUR in the framework of the 'Synchronisation and work-sharing' initiative, in which case a Core Safety Data Sheet should be prepared instead (see 3.4.3 above and the industry Q&A document on the HMA website).
- An overview of any safety measures taken anywhere in the world in the period covering the PSUR (if any),
- The sales volume of the product (see section 3.4.9),
- The calculated incidence rate as described in section 3.4.15,
- General details, such as names of the registration holder and of the product, registration number of the active substance... (most will already be in the SPC),
- An overview of all the AEs reported worldwide.

Besides the classic animal and human AEs, the following information must also be included, when available:

- Any AE in the literature that has been brought to your attention,
- Cases where the MRL values in edible products have been exceeded, even when the registered withdrawal periods have been respected,
- Potential environmental problems,
- Cases from post-authorisation studies (including clinical studies) using the marketed VMP),
- Lack of expected efficacy.

For additional information on the content of PSUR, you should also refer to Volume 9B<sup>6</sup>.

### 3.4.5 Which AE cases need to be included in the line listing?

The following reports must be included: spontaneous reports from your own country, from any other EU country and even outside the EU. They include all spontaneous reports on AEs, which occurred either in animals or humans, and any AEs reported directly to the CAs. Expedited cases from post-marketing safety studies should also be included. Even if you do not agree with the link assumed by the reporter between the case and your product, it must be reported. All these data should be presented in the so-called "line listing" format, as proposed in the guidelines.

### 3.4.6 What data need to be included for an AE reported in the line listing?

Focus should be made on the data of the reported cases. Whether a report should be considered as a real report depends on several parameters. The minimum data required to classify a report as a 'case' are given in 3.1.1.4 above. The data you will need to have available to enter a case in a line listing are the following:

- Company case reference number,
- National CA report reference number, if relevant,
- Date of treatment and date of reaction,
- Was the product used as recommended?
- Number of animals treated,
- Species and ages of the animals,
- Number of animals that reacted and eventually died,
- Concurrent use of other products,
- Narrative of the case, including clinical signs (using VeDDRA terminology – see also 3.1.2.15) and diagnosis,
- The ABON classification.

<sup>6</sup> Publication of final Volume 9B was pending at the time the GVPPG went to print; in the meantime, Volume 9 (June 2004) remains valid for veterinary medicinal products

### **3.4.7 What time span should the report cover? What is the common birth date?**

In order to streamline the reporting schedule and to prevent unnecessary reporting, the principle of the 'Common Birth Date' has been established. The first day of registration of a product in the EU is the European Birth Date. VMPs also authorised outside the EU have an International Birth Date (IBD), set as the date of the first MA granted in any country or region represented on VICH (whether members, i.e. EU, US and Japan or observers, i.e. Canada, Australia and New-Zealand). For VMPs first authorised in the EU, the EU Birth Date is the IBD. For administrative convenience and if desired by the MAH, the IBD may be designated as the last day of the same month. This birth date sets the time when your database should be closed or locked (Data Lock Point - DLP) for establishing the PSUR.

In order to harmonise periodic safety updates internationally, the MAH may use the IBD, rather than the EU Birth Date, to determine the DLPs in the EU; in such case, the first DLP must be within 6 months of the EU marketing authorisation Birth Date.

Each PSUR should cover the period of time since the last update report and must always be submitted within 60 days following the data lock point.

Dates for reports from nationally registered products will be defined by their national registration dates.

You should also refer to the agreed harmonised EU-DLPs as part of the 'PSUR synchronisation and work-sharing' initiative (see the list available from the HMA website at: <http://www.hma.eu/236.html>).

### **3.4.8 What language should be used?**

Overall, English should be used. Also for decentralised and national MAs, English is the language of choice. Moreover, most companies maintain their databases in English. A translation into a national language is inconvenient and might even negatively influence the consistency of the submitted data to the different MSs. Some countries may insist on receiving reports in their national language, but you have no obligation to do so. Also, submitting a report in the national language goes against the spirit of the EU database, EudraVigilance (see 4.3.3), whose language is English.

### **3.4.9 Must sales figures be provided for all MSs?**

Yes, sales volumes must be given on a country-by-country basis whenever possible.

### **3.4.10 For multiple species' products, how are sales attributed to one species?**

Scientifically, it is difficult to identify the proportion of your sales to species. The most logical solution is to provide one sales volume without going into speculations. However, some authorities will refuse a single sales figure for a multiple species' product. In such cases, a reasonable assessment should be possible, based on the information provided by your marketing department.

**3.4.11 How can the number of doses applied be calculated?**

In cases where you have a single dose product (e.g. vaccines) it is fairly simple, the number of doses sold in the PSURs period is the number of animals treated.

If your product has multiple dosing schedules and is eventually used in different breeds and age categories, it becomes difficult to identify the number of doses sold. In order to make a consistent report, leading to a consistent assessment, it is necessary to define upfront how the sales could actually relate to the number of animals treated.

The recommended way to achieve this is to put forward a justifiable formula taking into account the split of the sales over the different species and the different dosage regimens in each species. It is recommended to comment on the formula used to obtain the number of doses in the report.

In case of repeated administrations, the formula should also reflect whether or not each administration has been considered to be a single dose.

Furthermore, it is recommended to use standardised body weights for the animal species (see 3.4.12).

**3.4.12 What are the standardised body weights to be used in dose calculation formulae?**

The European authorities propose the following standard body weights:

Adult horse: ..... 550 kg

*Cattle*

Cow: ..... 550 kg

Newborn calf: ..... 50 kg

Beef calf: ..... 150 kg

*Sheep*

Adult sheep: ..... 60 kg

Lamb: ..... 10 kg

*Swine*

Sow/boar: ..... 160 kg (sow: 100; adult pig: 130)

Finishing pig: ..... 60 kg

Weaner: ..... 25 kg

Dog: ..... 20 kg

Cat: ..... 5 kg

For other species, IFAH-Europe proposes the following:

Broiler: ..... 1 kg

Layer: ..... 2 kg

Turkey: ..... 10 kg

Pigeons: ..... 30 pigeons/litre of drinking water

### 3.4.13 What AEs need to be included in incidence calculations?

Incidence rates should be based on ABO reports. Human cases, 'N' reports, suspected lack of expected efficacy cases, reports of violation of approved residue limits and environmental safety cases are to be excluded.

### 3.4.14 Do off-label AEs need to be included in incidence calculations?

Yes, you should include in your incidence calculation, all the cases, whether on or off-label cases that occurred in the target species.

### 3.4.15 Is there a standardised terminology to describe incidence rates?

IFAH-Europe recommends using the following convention:

- Very common ( $>1/10$ ),
- Common ( $>1/100, <1/10$ ),
- Uncommon ( $>1/1,000, <1/100$ ),
- Rare ( $>1/10,000, <1/1,000$ ),
- Very rare ( $<1/10,000$ ) or isolated cases.

## 3.5 ADVERSE EVENTS IN CLINICAL STUDIES?

### 3.5.1 Must cases occurring in post-authorisation safety studies be reported?

Studies set up to investigate specific safety issues related to a registered product, i.e. so-called 'post-authorisation safety studies' are described in section 7 of Volume 9B<sup>7</sup>. These studies exclude clinical trials for new indications, new methods of administration or new combinations, in which case you fall under the scope of off-label use. For this kind of study, you need a specific trial exemption in most member states and should address it before hand with the authorities of the MS(s) where the trials will be carried out.

### 3.5.2 How must cases occurring in clinical studies with unlicensed products be handled?

In principle, this is handled by the guidelines on Good Clinical Practice (GCP), which are based on the VICH guidelines. Detailed guidance can be found in the GCP handbook available from IFAH-Europe.

Furthermore, this issue is regulated by the national CAs when issuing trial clearances.

In general, it can be said that when drafting a protocol for a trial, it is essential that the AE section is assessed thoroughly. Often immediate actions are required and good and clear instructions are paramount in such cases.

A good principle is to record as much as possible. In case of doubt, record and investigate it as an AE. This data might be very helpful in the final benefit/risk assessment of your new product.

<sup>7</sup> Publication of final Volume 9B was pending at the time the GVPPG went to print; in the meantime, Volume 9 (June 2004) remains valid for veterinary medicinal products



# 4 TOOLS

## 4.1 QUALIFIED PERSON FOR PHARMACOVIGILANCE (QPPV)

It is a legal requirement to have permanently and continuously at your disposal a Qualified Person responsible for pharmacovigilance (QPPV); this person must reside in the EU (see articles 74 of Directive 2001/82/EC, as amended by Directive 2004/28/EC and Article 48 of Regulation 726/2004). The qualification and experience required are not defined in the legislation and most countries have their own system where focus is often on a scientific/medical background in combination with a certain experience with pharmacovigilance. The QPPV is the main contact point, both internally and externally, for all company pharmacovigilance information; the QPPV must be registered with EudraVigilance Vet (see 4.3 Electronic reporting). He/she also informs the authorities and provides them with any additional information they might require. The current legislation also foresees inspections of the PhV system for which the QPPV is responsible.

## 4.2 COMPANY PHARMACOVIGILANCE SYSTEM

### 4.2.1 Does a company need a PhV system?

Yes, companies must ensure that they have a reliable system for collecting and collating information on adverse reactions, i.e. an adverse event database. This system, which can either be set up internally or contracted out,

must guarantee that information about all AEs, which are reported to the personnel of the company, including representatives, is collected and collated so that it may be accessed from at least one point within the Community. Obviously, when you have a database in which you lodge specific data on individuals, this database is subject to the legislation on databases and the protection of privacy.

Furthermore, a detailed description of your system must be included in your dossier when submitting applications for marketing authorisation (see 2.3).

### 4.2.2 Does the pharmacovigilance system (adverse event database) need to be digital?

No, the guidelines only make it obligatory to have a system that allows reporting in an electronic way in accordance with the format and specifications as they are defined in the GLs. Nevertheless, experience indicates that digital systems may be more convenient and reliable (prevent loss of data, facilitate data analysis...).

### 4.2.3 Must the system be accessible from within every single EU Member State?

No, the system should have at least one point of access within the Community, but one point is sufficient. The company can choose the location of this point.



#### **4.2.4 Do I have to inform the authorities of how I organise my PhV activities?**

It is not necessary to systematically provide information on the organisation of your pharmacovigilance activities. However, when you apply for a new marketing authorisation, it is obligatory to provide a detailed description of your pharmacovigilance system in the dossier.

#### **4.2.5 What are the consequences if I do not fulfil my PhV obligations?**

Pharmacovigilance is based on responsibility and trust. If you do not have an appropriate system in place, you miss on an opportunity to enhance the cooperation and relation with your customers and CAs. Whilst this should be enough to encourage any license holder to fully assume its responsibility, the CAs have foreseen the possibility to inspect companies' systems and eventually apply significant penalties to those not fulfilling their legal duties. While this can be regretted in view of the open attitude advocated by IFAH-Europe and its members, the possible consequences should not be taken lightly.

### **4.3 ELECTRONIC REPORTING: EUDRAVIGILANCE**

#### **4.3.1 Do I need to report all AEs electronically?**

At the present time, only serious AEs have to be reported within 15 days and electronically, except under exceptional circumstances. The detailed schemas for the electronic reporting of such cases are available from the EMA EV Vet website.

See: <http://eudravigilance.ema.europa.eu/veterinary/reporting.html>.

#### **4.3.2. How do I submit electronically?**

This is achieved using EudraVigilance Veterinary (EV Vet) for which you should register at the following:

<http://eudravigilance.ema.europa.eu/veterinary/register.html>.

EV Vet is the European data-processing network and database management system for the exchange, processing and evaluation of AE reports related to VMPs authorised in the EEA. EV Vet provides three different ways of electronic reporting, depending on the number of reports and/or the size of your company:

##### **➔ Gateway**

If you have a company database you can submit via the Gateway. The Gateway is a separate software package developed by third party IT software companies in accordance with specific requirements and allows the pharmaceutical industry to report to a common reporting point within the EEA. Typically, your IT department will be in charge of setting-up the Gateway to ensure compatibility between your local system and EudraVigilance Veterinary. On a day-to-day basis, you will continue to work with your local system for the data input that are distributed over the Gateway.

For other companies, there are 2 other options:

##### **➔ EVWeb**

This is a web interface that allows the user to manually create and upload AE reports and products' messages. From EVWeb you can send information securely to one or more CAs, specific MAHs and/or the central database depending on the type of information.

##### **➔ Simple form**

The MAH Simple Electronic Form is a reporting module that has been developed for use by MAHs with a limited number of reports. Its use is to be agreed upon with your national CA. It is a web-based form that allows you to create an AE report related to a VMP



with the use of standard terminology. The form is available from the EMA EV Vet website – see:

<http://eudravigilance.ema.europa.eu/veterinary/mahsimplified.html>

#### **4.3.3 What is the purpose of EudraVigilance Vet?**

EudraVigilance Vet is a key component in supporting the MSs and the EMA within its scientific committees in the co-ordination of the supervision, under practical conditions of use, of VMPs authorised within the EEA. It also provides advice on the measures to ensure the safe and effective use of these products, in particular by evaluating and making available through a pharmacovigilance database, information on AEs.

### **4.4 WRITTEN PROCEDURES ON VETERINARY PHARMACOVIGILANCE**

#### **4.4.1 Should every company have a written procedure on veterinary pharmacovigilance?**

The legislation stipulates that a detailed description of your PhV system must be included in your MA application. It is clear that a written procedure will help to comply with this requirement. Written procedures can help your company to ensure that the pharmacovigilance process is up to high quality standards. Furthermore, they help to overcome shortcomings in the process. Make sure everyone in the company is informed of these procedures and their implications.

#### **4.4.2 What considerations should be taken into account when writing a procedure on pharmacovigilance?**

When writing a procedure, all legal requirements should be taken into account, as well as internal company requirements,

though internal requirements can never overrule legal ones. Procedures should be developed in such a way that they fit the legal timeline requirements. Procedures should at least address the definition of an AE, as well as the recording, investigation and reporting procedures for AEs within the company.

#### **4.4.3 Is it necessary to train relevant company personnel in pharmacovigilance procedures?**

Yes, training of relevant personnel will not only demonstrate to the CAs that the company is fulfilling its obligations; it will also contribute to a higher quality pharmacovigilance system. It should also be remembered that it is best having a flexible and practical SOP rather than a more stringent one that will not be followed.

### **4.5 CAN PHARMACOVIGILANCE BE SUBJECT TO INSPECTIONS?**

Yes, any of the items described above, i.e. your company DDPS, SOPs, electronic reporting system (including your database), can be subject to a targeted or routine inspection.

Such inspections can be carried out nationally or be mandated by the EMA/CVMP (EU inspection). The competent authority for inspection is generally the competent authority of the Member State in whose territory the MAH QPPV is located, unless an additional facility in another MS also needs inspecting. These are further described in the EU guideline on monitoring of compliance with pharmacovigilance regulatory obligations and pharmacovigilance inspections for veterinary medicinal products.

# IMPROVING REPORTING AND COMMUNICATING PHARMACOVIGILANCE INFORMATION

Pharmacovigilance information is not easy to communicate. No one likes to discuss “unpleasant” experiences occurring with their products. Furthermore, reporters do not always appreciate the benefits from reporting to the MAH or are even afraid to do so and CAs may have, understandably, doubts as to whether all necessary actions have been taken. For these reasons, it is important to assess what can be done to improve external communications and consequently the output of pharmacovigilance information.

## 5.1 HOW CAN REPORTING BE GENERALLY IMPROVED?

In principle, anyone can report an AE. In practice, however, not only the number of reports, but also the quality of the data, should be taken into consideration. In this respect, it seems obvious that your efforts should be directed towards the veterinary profession. This group is scientifically qualified and also has an important interface with what is really occurring under field conditions. Their ongoing support and understanding will increase the number and above all the quality of reports.

## 5.2 HOW CAN CUSTOMERS AND END USERS BE CONVINCED OF THE IMPORTANCE TO REPORT?

As already mentioned above, the most valuable partner is the veterinary profession. Unfortunately, it is not always easy to convince this group of the importance of reporting AEs, as their daily priority is to give assistance to their customers and not to fill in forms. Ne-

vertheless, for the success and effectiveness of pharmacovigilance, it is important to increase awareness and encourage the cooperation of the veterinary profession. The systematic reporting of AEs will result in better treatments. This will benefit not only the veterinary profession, but also their customers and patients. Improved label information will reduce the incidence of adverse reactions, which has a direct benefit on animal welfare. Improving animal welfare falls within the high ethical values of veterinarians. When communicating with a reporter, keep in mind the following aspects:

- A reporter is entitled to a fast and personalised reply.
- Good and scientific assistance is always appreciated.
- Provide the reporter with clear instructions on where and how your company can be reached in case of AEs.
- Always keep the reporter informed of the final outcome: feedback is very valuable to the veterinarian.
- Money should never be offered to encourage reporting!

To also promote reporting from the veterinary profession, the EMA/CVMP has developed a common EU reporting form and a Simple Guide to Veterinary Pharmacovigilance<sup>8</sup> aimed at veterinarians and other animal health professionals; it also contains a reporting form in all EU languages.

## 5.3 HOW CAN THE BEST INFORMATION BE OBTAINED?

It is indeed crucial that good quality data is provided. Three major points must be taken into account by making sure of the following:

<sup>8</sup> Veterinary Pharmacovigilance in the EU – A Simple Guide to Reporting Adverse Reactions [EMA/CVMP/PhVWP/110607/2005] [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Scientific\\_guideline/2009/10/WC500004990.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/10/WC500004990.pdf)

- Follow-up the case personally.
  - Obtain as much data as possible as quickly as possible. The best quality data is obtained when the case is “fresh”.
  - Obtain all the data. Again, a personal follow up is essential for this.
- The key aspect is to be open in your communication.

#### 5.4 WHAT CONSIDERATIONS SHOULD BE TAKEN INTO ACCOUNT WHEN COMMUNICATING WITH THE AUTHORITIES?

Obviously, all the legal requirements described above, must be well respected, but good pharmacovigilance practice goes further. Again, make sure you are open and pro-active in the way you communicate and keep the following in mind:

- ➔ Report early: it is best sending in a very brief report at an early stage and completing the full data set later, rather than waiting until you think you have all the required information. By then, it is more difficult to retrieve additional data should the CAs request it. Also if authorities consider an action is required, they should be informed early.
- ➔ Make sure all communications are clear and informative. Avoid standard statements.
- ➔ When optimising relationships with CAs by clear and open communication, companies will also increase the likelihood of (pro) active communication of potential problems by the CAs to the companies.

#### 5.5 IS INTERNAL COMMUNICATION IMPORTANT?

Pharmaceutical companies are often large structures composed of different departments with different interests. It is important that the right information on pharmacovigilance circulates internally. Make sure this communication is positive. After all, good pharmacovigilance provides valuable

information on your products, which is beneficial to the whole company. Also make sure that good and clear instructions on your policy are circulated and well known. It will enhance good reporting and will provide guarantees that reports are handled in the best possible way. This is best accomplished by formal training on the company pharmacovigilance procedures.

#### 5.6 WILL MY REPORTS BE MADE AVAILABLE TO THE GENERAL PUBLIC?

To address the growing importance of PhV, and as part of its increased transparency strategy, the CVMP, based on all the relevant information about AEs, may draw up opinions on the necessary measures, which may include amendments to the MA. These opinions are made available to the public. Furthermore, the Agency is responsible for ensuring the dissemination of information on AEs by means of a database permanently accessible to all MSs and with the public being given appropriate level of access [Article 57(d) of Regulation 726/2007]. Appropriate PhV information must also be made available to the public [Article 57(f) of Regulation 726/2007]. Such level of access will be described in more detail in the EMA Eu-draVigilance Vet access policy for medicines for veterinary use.

Since 2004, EMA also publishes annual Public Bulletins on Veterinary Pharmacovigilance, which aim to improve communication with stakeholders and particularly veterinary health professionals on the safety of VMPs in the EU.

#### 5.7 CAN I COMMUNICATE MY PHV DATA TO THE GENERAL PUBLIC?

Yes, you can communicate PhV information to the general public, but such information is not to be used for promotional purposes and you should first notify the relevant CA(s) should you wish to do so.

# LIST OF ABBREVIATIONS

ABON	A: probable B: possible	O: unclassifiable N: unlikely
AE	Adverse Event	
CA(s)	Competent Authority(ies)	
CVMP	Committee for Veterinary Medicinal Products	
DCP	Decentralised Procedure	
DDPS	Detailed Description of the Pharmacovigilance System	
DLP	Data Lock Point	
EMA	European Medicines Agency <a href="http://www.ema.europa.eu">http://www.ema.europa.eu</a>	
EU	European Union	
EEA	European Economic Area	
EV Vet	EudraVigilance Veterinary <a href="http://eudravigilance.ema.europa.eu/veterinary">http://eudravigilance.ema.europa.eu/veterinary</a>	
FVE	Federation of the Veterinarians of Europe <a href="http://www.fve.org">http://www.fve.org</a>	
GCP	Good Clinical Practice	
GL	Guideline	
GMP	Good Manufacturing Practice	
GVPPG	Good Veterinary Pharmacovigilance Practice Guide	
IBD	International Birth Date	
IFAH-Europe	International Federation for Animal Health-Europe <a href="http://www.ifaheurope.org/">http://www.ifaheurope.org/</a>	

MA	Marketing Authorisation
MAH(s)	Marketing Authorisation Holder(s)
MIC	Minimum Inhibitory Concentration
MRL	Maximum Residue Limit
MRP	Mutual Recognition Procedure
MS(s)	Member State(s)
PMS	Post-Marketing Study
PSURs	Periodic Safety Update Reports
PhV	Pharmacovigilance
QA	Quality Assurance
QP	Qualified Person
QPPV	Qualified Person for Pharmacovigilance
RMS	Reference Member State
SLEE	Suspected Lack of Expected Efficacy
SOP	Standard Operating Procedure
SPC	Summary of Products Characteristics
VICH	International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Products <a href="http://www.vichsec.org/">http://www.vichsec.org/</a>
VeDDRA	Veterinary Dictionary for Drug Regulatory Affairs <a href="http://eudravigilance.ema.europa.eu/veterinary/documentation.html">http://eudravigilance.ema.europa.eu/veterinary/documentation.html</a>
VMP	Veterinary Medicinal Product

# 7

## APPENDIXES

### APPENDIX 1: LEGAL TEXTS AND OFFICIAL DOCUMENTS

#### VOLUME 5 - PHARMACEUTICAL LEGISLATION MEDICINAL PRODUCTS FOR VETERINARY USE<sup>9</sup>

- Directive 2004/28/EC of the European Parliament and of the Council of 31 March 2004 amending Dir. 2001/82/EC on the Community code relating to veterinary medicinal products [Official Journal L 136, 30.04.2004 p. 58]
- Regulation 726/2004 of the European Parliament and of the Council laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency [Official Journal L 136, 30.04.2004, p. 1]
- Commission Directive 91/412 laying down the principles and guidelines of good manufacturing practice for veterinary medicinal products [Official Journal L 228, 17.08.1991 p. 70]
- Directive 2009/53/EC of the European Parliament and of the Council of 18 June 2009 amending Directive 2001/82/EC and Directive 2001/83/EC, as regards variations to the terms of marketing authorisations for medicinal products. [Official Journal L 168, 30/6/2009, p. 33]
- Commission Regulation (EC) No 1234/2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products, was published in the Official Journal of the European Union [Official Journal L 334, 12.12.2008, p. 7]

#### VOLUME 6 - NOTICE TO APPLICANTS AND REGULATORY GUIDELINES FOR MEDICINAL PRODUCTS FOR VETERINARY USE<sup>10</sup>

- Guideline on the details of the various categories of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products [Official Journal 2010/C 17/01]
- Guideline on the operation of the procedures laid down in Chapters II, III and IV of Commission Regulation (EC) No 1234/2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products [Official Journal 2009/C 323/04]

#### VOLUME 9B - GUIDELINE ON MONITORING OF COMPLIANCE WITH PHARMACOVIGILANCE REGULATORY OBLIGATIONS AND PHARMACOVIGILANCE INSPECTIONS FOR VETERINARY MEDICINAL PRODUCTS<sup>11</sup>

NOTE: pending the release of final volume 9B, Volume 9 (both human and veterinary) made public in June 2004 remains valid for medicinal products for veterinary use.

#### EMA/CVMP GUIDELINES AND DOCUMENTS

- EMA: <http://www.ema.europa.eu> - sections Regulatory / Veterinary Medicines /
  - Pharmacovigilance (left hand column) and
  - Post-authorisation / Procedural Q&A (left hand column)
- EMA EudraVigilance Vet: <http://eudravigilance.ema.europa.eu/veterinary>

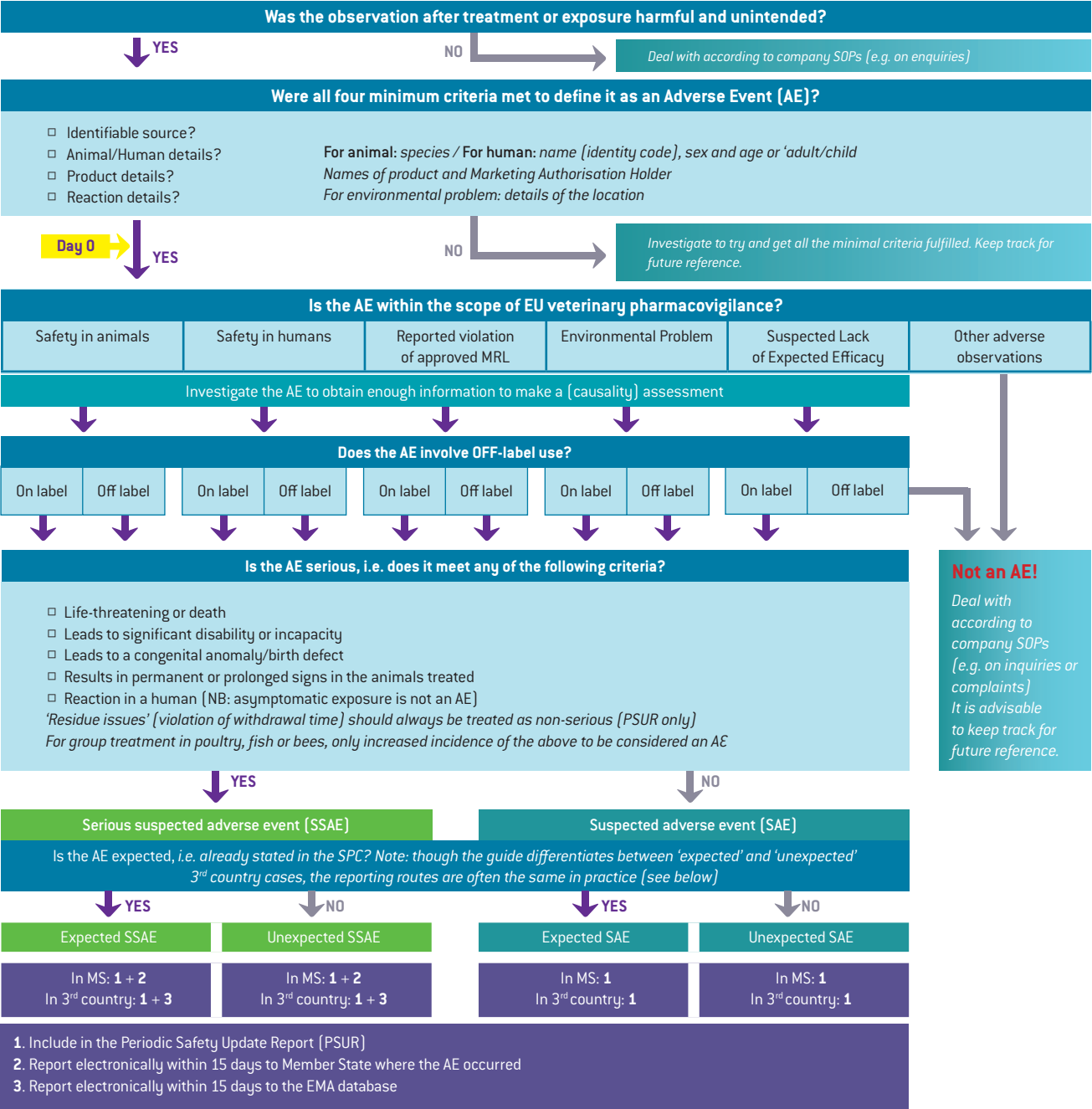
VICH <http://www.vichsec.org/>

<sup>9</sup> [http://ec.europa.eu/enterprise/sectors/pharmaceuticals/documents/eudralex/vol-5/index\\_en.htm](http://ec.europa.eu/enterprise/sectors/pharmaceuticals/documents/eudralex/vol-5/index_en.htm)

<sup>10</sup> [http://ec.europa.eu/health/documents/eudralex/vol-6/index\\_en.htm](http://ec.europa.eu/health/documents/eudralex/vol-6/index_en.htm)

<sup>11</sup> [http://ec.europa.eu/health/documents/eudralex/vol-9/index\\_en.htm](http://ec.europa.eu/health/documents/eudralex/vol-9/index_en.htm)

APPENDIX 2: DECISION TREE WHEN A REPORT IS RECEIVED ON AN OBSERVATION AFTER TREATMENT OR EXPOSURE TO A VMP







**International Federation for Animal Health-Europe AISBL**

Rue Defacqz, 1  
1000 Brussels  
Belgium

T +32 (0)2 543 7560  
F +32 (0)2 537 0049

info@ifahaurope.org  
[www.ifahaurope.org](http://www.ifahaurope.org)



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