

Guidance for Industry

Pharmacovigilance of Veterinary Medicinal Products: Management of Adverse Event Reports (AER's) - VICH GL24

DRAFT GUIDANCE

This guidance document is being distributed for comments only

This draft guidance document describes a system for the management of adverse drug event reports following the use of marketed veterinary medicinal products.

Comments and suggestions regarding the document should be submitted to Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://www.regulations.gov>. All comments should be identified with the Docket No. 2000D-1632.

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**U.S. Department of Health and Human Services
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PHARMACOVIGILANCE OF VETERINARY MEDICINAL PRODUCTS – MANAGEMENT OF ADVERSE EVENT REPORTS

Recommended for Consultation

at Step 4 of the VICH Process

on 2 November 2005

by the VICH Steering Committee

This Guidance has been developed by the appropriate VICH Expert Working Group and is subject to consultation by the parties, in accordance with the VICH Process. At Step 7 of the Process the final draft will be recommended for adoption to the regulatory bodies of the European Union, Japan and USA.

**PHARMACOVIGILANCE OF VETERINARY MEDICINAL PRODUCTS
Management of Adverse Event Reports**

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***Contains Non-Binding Recommendations
Draft—Not for Implementation***

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I.

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Introduction

Pharmacovigilance of veterinary medicinal products (VMPs) can be defined as the detection and investigation of the effects of the use of these products, mainly aimed at safety and efficacy in animals and safety in people exposed to the products. This document will only deal with the spontaneous reporting system for identification of possible adverse events following the use of marketed VMPs.

Within all regions involved in the VICH process there are certain legal obligations for the pharmaceutical industry, the commercial party responsible for the products, with regard to adverse events reported to them. Those legal obligations relate to the acceptance of adverse event reports and the storage and submission of those reports to the authorities.

It is of importance for all parties, the Marketing Authorization Holders (MAHs), the Regulatory Authorities (RA) and the users of VMPs to develop harmonized and common systems, common definitions and standardized terminology within pharmacovigilance. Harmonization of those elements between the regions facilitates the reporting responsibilities for the MAHs, many with worldwide activities. At the same time harmonization of systems and requirements facilitates the inter-regional comparison of data and exchange of information, thereby increasing the general knowledge of a product's general performance and safety profile.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word "should" in Agency guidances means that something is suggested or recommended, but not required.*

II. Scope

The scope of pharmacovigilance in this VICH document is defined as the management of the detection and investigation of the clinical effects of marketed VMPs mainly concerned with the safety and efficacy in animals and the safety in people exposed to these products. While pharmacovigilance in its broadest sense may entail a wide range of activities, this document only deals with the spontaneous reporting system for the identification of possible adverse events following the use of marketed VMPs.

* Under 21 CFR 10.115(i)(3), when issuing draft guidance documents that are the product of international negotiations, FDA need not apply 21 CFR 10.115(i)(2), which states that guidance documents must not include mandatory language such as "shall," "must," "required," or "requirement," unless FDA is using these words to describe a statutory or regulatory requirement. However, any final guidance document issued according to 21 CFR 10.115(i) must contain the elements in 21 CFR 10.115(i)(2). In this draft guidance, any language that is mandatory under U.S. laws and/or regulations is followed by a citation to the appropriate statutory or regulatory provision. In accordance with 21 CFR 10.115(i)(3), any mandatory language in this draft guidance that does not describe a statutory or regulatory requirement will be revised in the final guidance document to comply with 21 CFR 10.115(i)(2).

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III. Definitions

The terms and definitions in this document are intended to harmonize other previously used terms referring to similar concepts. Within the scope of this document the following definitions of items or actions have been developed.

III.1 Veterinary Medicinal Product (VMP)

Any medicinal product with approved claim(s) to having a protective, therapeutic or diagnostic effect or to alter physiological functions when administered to or applied to an animal. The term applies to therapeutics, biologicals, diagnostics and modifiers of physiological function. (For the definitions of "drug" and "new animal drug" in the U.S., see 21 U.S.C. 321(g)(1) and (v).)

The "same biological VMP" is defined as originating from the same MAH being responsible for pharmacovigilance of this/these VMPs with same manufacturing specifications.

The "same pharmaceutical VMP" is defined as originating from the same MAH being responsible for pharmacovigilance of this/these VMPs with same formulations.

A "similar pharmaceutical VMP" is defined as:

- originating from the same MAH being responsible for pharmacovigilance of this/these VMPs,
- the same active ingredients,
- major excipients with the same or similar pharmaceutical function,
- at least one common registered species.

III.2 Adverse Event (AE)

An adverse event is any observation in animals, whether or not considered to be product-related, that is unfavorable and unintended and that occurs after any use of VMP (off-label and on-label uses). Included are events related to a suspected lack of expected efficacy according to approved labeling or noxious reactions in humans after being exposed to VMP(s). (See 21 C.F.R. 514.3 for the definition of an adverse drug experience in the U.S.)

An AE may at some point be concluded by a RA to be an adverse reaction when there is at least a reasonable possibility (i.e., relationship cannot be ruled out) that harmful and unintended observations were a response to a VMP administered at doses normally used in animals for prophylaxis, diagnosis or therapy of disease or for modification of physiological function.

III.3 Serious Adverse Event

A serious adverse event is any adverse event which results in death, is life-threatening, results in persistent or significant disability/incapacity, or a congenital anomaly or birth defect. (See 21 C.F.R. 514.3 for the definition of a serious adverse drug experience in the U.S.)

For animals managed and treated as a group, only an increased incidence of serious adverse events as defined above exceeding the rates normally expected in that particular group is considered a serious adverse event.

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III.4 Unexpected Adverse Event

An unexpected adverse event is an adverse event of which the nature, severity or outcome is not consistent with approved labeling or approved documents describing expected adverse events for a VMP. (See 21 C.F.R. 514.3 for the definition of an unexpected adverse drug experience in the U.S.)

III.5 Adverse Event Report (AER)

An adverse event report is a direct communication from an identifiable first-hand reporter (see IV.7) that includes at least the following information:

- an identifiable reporter
- an identifiable animal(s) or human(s)
- an identifiable VMP
- one or more adverse events

One animal or one human being, or a medically appropriate group exhibiting similar clinical signs should be included in a single report.

III.6 Marketing Authorization Holder (MAH)

The Marketing Authorization Holder is the commercial party who, according to the RA is responsible for the pharmacovigilance of the VMP. (See 21 CFR 514.80 for requirements on establishing, maintaining, and reporting required information relating to experiences with a new animal drug, defined in 21 U.S.C 321(v).)

III.7 Regulatory Authority (RA)

The Regulatory Authority is the national or regional authority which, according to the legislation, is responsible for the issuing, adaptation or withdrawal of marketing authorizations/licences of VMPs and for pharmacovigilance activities. (See 21 U.S.C 360b.)

III.8 Periodic Summary Update (PSU)

The document submitted to the RA at set intervals to support the continued marketing and the adequacy of the approved labeling of the VMP and will include an analysis of all AERs received during the interval. (See 21 C.F.R. 514.80 for periodic drug experience report requirements in the U.S.)

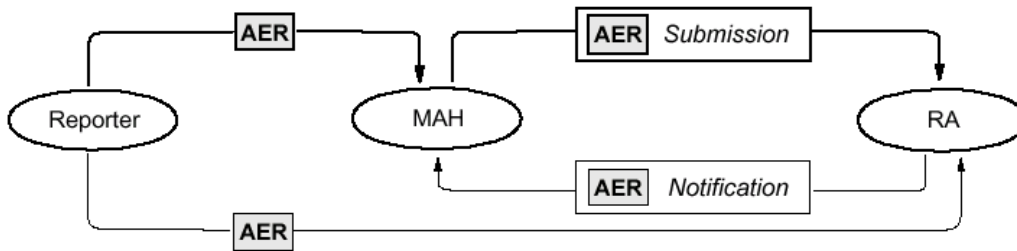
III.9 International Birth Date

International Birth Date (IBD) is the date of the first marketing authorization for same or similar product granted in any VICH region.

IV. The Pharmacovigilance Process

IV.1 Information Flow in the Pharmacovigilance System.

The flow of information is illustrated below:



Information Flow in the Pharmacovigilance System.

Data preferably flows as shown in the upper half of the figure, where the reporter communicates with the MAH and the MAH submits AERs it has received to the RA. An alternate path is shown in the lower half, where the reporter communicates with the RA and the RA notifies the MAH of AERs it has received.

IV.2 Informational Unit

The basic unit of information in the pharmacovigilance system covered by this document is the AER.

IV.3 Recording AERs

The MAH should record each AER received and store it in a manner which allows easy access to the data. The receipt, acknowledgement or recording of an AER by the MAH or the RA does not necessarily have any implication regarding the veracity or authenticity of the AER nor implies any degree of causality. See 21 C.F.R. 514.80 for recordkeeping requirements in the U.S.

IV.4 Submitting AERs

The MAH must submit an AER to regional authorities as provided by relevant laws or legislation either as an expedited submission or as a periodic submission. See 21 C.F.R. 514.80 for reporting requirements. The submission of an AER does not necessarily imply an endorsement or agreement with its content, unless regional or national regulations require differently.

IV.5 Expedited AER Submissions

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Expedited submission of certain AERs may be required (see 21 CFR 514.80), related to the seriousness or unexpectedness of the reported event or because of the urgency of its implications regarding the safety of animals or man.

Expedited submission to RAs in other VICH regions/observer countries will occur when:

- an AER is an expedited submission in the country where the AER occurs and
- the same VMP is approved in other VICH regions/observer countries and
- the species of animal involved in the AER is a species approved in the other VICH regions/observer countries or
- there are serious implications regarding human safety

The timeclock for the expedited submission to RAs in other VICH regions/observer countries begins when the AER becomes the knowledge of the MAH within the other region. A follow-up submission will occur when the investigation of the AER is completed by the MAH in the country where the AER occurred.

If, based on these expedited submissions, the RA decides on a regulatory action, the MAH will immediately inform all VICH regions/observer country RAs where the same VMP is approved about this action.

In addition, when the MAH determines that it is likely that actions will be implemented based on the AERs it has received, the MAH will contact all VICH regions/observer RAs where the same VMP is approved to inform them of the MAH concerns and its likely actions.

IV.6 Periodic AER Submissions

At regular intervals, the MAH must submit all AERs not previously submitted. See 21 C.F.R. 514.80 for periodic drug experience report requirements in the U.S.

IV.7 Reporting Source

Although reporting via the attending veterinarian is encouraged, an AER may be initiated by anyone directly involved with the purported adverse event. Preferably, an AER is communicated by the reporter directly to the MAH, but the AER may also have been routed through an agent or the RA. A communication through an intermediate agent should be considered an AER only if the agent has been authorized by the reporter and provides sufficient information to allow direct contact between the reporter and the MAH.