European Medicines Agency
Inspections

London, 27 November 2009
Doc. Ref.: EMEA/INS/PhV/384646/2008

Pharmacovigilance Inspection Policy for Centralised Procedures- Medicinal Products for Veterinary Use

1. Background

Pharmacovigilance (PhV) inspections are performed to ensure that the Marketing Authorisation Holders (MAHs) for Centrally Authorised Products (CAPs) comply with PhV regulatory obligations and to facilitate compliance.

2. Objectives

This document sets out the policy on the basis of which PhV inspections relating to the Centralised Procedure should be requested. The policy should:

- Provide for both routine and targeted inspections.
- Provide a sufficient number of inspections to enable the assessment of the monitoring of compliance with PhV obligations of the MAHs with CAPs.
- Lead to a number and range of PhV inspections that allows data to be generated on inspection findings and communicated in a public (anonymised) manner, so that the community can be aware of problems giving rise to PhV non-compliance.
- Lead to a sufficient "risk" of inspection that acts as a reasonable deterrent to poor compliance or malpractice.
- Increase the awareness of the need for, and actual compliance with the MAH PhV obligations
- Make productive use of PhV inspection resource in the interests of the Community.
- Provide for increased predictability in the numbers of inspections, so that workload and resource requirements are more predictable, for the Member State inspectorates.

3. Legal Framework for PhV inspections in the Context of the Centralised procedure

The legal basis for PhV inspection for veterinary medicinal products is set out in article 80 of Directive 2001/82/EC which gives the competent authorities of the Member States (MS) powers to inspect the premises, records and documents of MAHs or any firms performing the activities described in Title VII of that directive, and in particular Articles 74 and 75 thereof, on behalf of an MAH. These inspections are recognised by all MS in accordance with article 90 of Directive 2001/82/EC.

Section 5, of the guideline on monitoring of compliance with PhV regulatory obligations and PhV inspections for veterinary medicinal products published as a standalone guideline under Volume 9B of the Rules Governing Medicinal products in the European Union sets out further details regarding the responsibilities, organisation, conduct and reporting of such inspections. In particular it requires that the Committee for Veterinary Medicinal Products (CVMP), the PhV Working Party (PhV WP) and the PhV Inspectors Working Group (PhV IWG), in conjunction with the Competent Authority of the MS in whose territory the MAH's Qualified Person for Pharmacovigilance (QPPV) is located, determine a programme for inspection in relation to CAPs. These inspections are to be prioritised based on the potential risk to animal and public health, the nature of the products, extent of use, number of products that the MAH has on the EEA market and other factors.

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 8595
E-mail: mail@emea.europa.eu http://www.emea.europa.eu

4. Inspection Programmes

As outlined in the guideline on monitoring of compliance with PhV regulatory obligations and PhV inspections for veterinary medicinal products under Volumes 9B, MS inspectorates will implement programmes of PhV inspections and it is anticipated that national inspection programmes will in many cases fulfil the need for the routine inspections of the CVMP programme for CAPs. Therefore when a Competent Authority has carried out, or intends to carry out an inspection covering the scope and within the timeframe requested by the CVMP programme, that inspection will suffice and its results will be made available to the CVMP and to the other applicable competent authorities concerned by that PhV system.

These CVMP programmes will be agreed by the PhV IWG, PhV WPs and adopted by the CVMP and its preparation will be as outlined in the "Procedure for the preparation of a risk-based programme for routine PhV inspections of MAHs connected with CAPs."

There will be situations where these inspections might be specifically requested by the CVMP (e.g. global PhV sites in third countries).

The EMEA secretariat (Inspections sector) will maintain an overview of the inspection programme and of the routine and targeted inspections adopted and conducted. Statistics on the conduct of the inspection programme, covering both routine and targeted inspections will be made available to the PhV IWG, PhVWP and CVMP.

5. Routine and Targeted inspections

Routine and targeted inspections are defined in section 5 of the guideline on monitoring of compliance with PhV regulatory obligations and PhV inspections for veterinary medicinal products under Volume 9B. Routine inspections form the basis of an ongoing programme of monitoring of compliance of MAHs. Targeted inspections may be requested, as one possible regulatory action, in response to specific issues arising where there is a potential for increased risk of non-compliance or where there are indications that the PhV system or reporting may be non-compliant.

6. Relation target/routine inspections

There is a potential overlap in activity between a routine and a targeted inspection. The relationship between these two types of inspections needs to be considered. In principle a targeted inspection will replace the need for a routine inspection and therefore once a targeted inspection is requested the scheduled routine inspection will be postponed in accordance with the schedule.

There will be situations where it would be better, rather than requesting a targeted inspection, to ask questions to the MAH and then review the specific responses and actions taken as part of the forthcoming routine inspection.

If a targeted inspection is necessary and requested when a routine inspection has been performed recently, the inspection request should focus on the particular triggers for that targeted inspection and not other aspects of the system.

It is assumed that in most cases targeted inspections will result as a direct request from the assessors/CVMP. These inspections should be given priority due to their nature of investigating an established concern and a targeted inspection will replace the need for a routine inspection.

7. Inspection Team

The Competent Authority for inspection of the MAH's PhV system will be the Competent Authority of the MS in whose territory the MAH's QPPV is located. Where an additional facility (e.g. a database) in another MS requires inspection, the inspection will be carried out by the Competent Authority of the MS in whose territory the facility is located and could be a joint inspection involving the inspectorate of the MS where the QPPV is located.

In general, companies have a PhV centre in the Community covering multiple products that are on the market, in the Community. These centres may also be the global PhV centres, or the latter may be located in third countries. Where the global centres, databases etc. are located in third countries, the same Competent Authority as above will be responsible for purposes of inspection on behalf of the community, if such an inspection is considered necessary. Where relevant or on request, and in particular for product-specific issues, they may be assisted, or the inspection may be conducted, by an inspector and/or expert from the Rapporteur/Co-Rapporteur Member State.

It is usual that the inspection team at any one site being inspected is made up of two inspectors, who may come from the same or different inspectorates. For CVMP inspection requests, it is preferable that inspectors from two agencies participate to increase the process of harmonization.

In addition, a clinical expert may accompany the inspection team. Additional inspectors may work on a group of sites. Inspectors may attend as observers for training purposes, usually at the cost of their agency.

8. Inspection scope

The scope of each inspection request and the number of sites should be well focused so that the key objectives are met. In this respect a key aspect of the inspection scope will depend on whether or not it is a system or product related inspection (these are described in sections 5.4 and 5.5, respectively, of the Volume 9B "Guidelines on Pharmacovigilance of veterinary medicinal products").

Taking this into account, three scenarios are possible:

1. A routine system inspection, in which CAPs are selected to provide examples of the functioning of the PhV system. The factors to be considered for deciding this type of inspections are described in Annex 1 of the procedure for the preparation of a risk-based programme for routine inspections of MAHs connected with CAPs.

2. A targeted inspection, which includes a review of the PhV system. The factors to be considered for deciding this type of inspections are described in Annex 2 of the procedure for the preparation of a risk-based programme for routine inspections of MAHs connected with CAPs.

3. A targeted product-specific inspection conducted to address specific questions, which does not include a systems review e.g. because the PhV system has recently been examined. In which case this inspection may not replace a planned routine systems inspection, unless the latter is planned within a short timeframe of the former.

In the preparation of the scope of the CVMP request it should be ensured that:

- EMEA receives feedback from the inspectors and assessors on the draft scope of the inspection and selection of sites to be inspected in order to ensure that the questions are the most appropriate for the inspectors to answer, and that the sites are the appropriate ones to inspect in that context.

- Communicate with the inspectors and assessors in relation to previous inspections in order to reach a final decision on the real needs for the inspection or to determine if the issue should be followed up with questions addressed to the MAHs.

9. Site selection

In the selection of sites for a CVMP inspection request consideration should be given to the following:

- Information on previous EU inspections is needed in order to avoid unnecessary repeated inspections of the same sites, review of the same system or interview of the same people.

- Third country sites should only usually be inspected where some processes are performed in third countries and there is a specific need to inspect these processes. It may be appropriate to inspect for education purposes or for interviewing personnel performing certain activities.

- Exchange of information with the MAH on what information is available at the QPPV site and at the third country sites. If doubts arise about the selection of a third country site for inspection, then the inspection request will be adopted without that site and amended later to include that site if recommended by the inspector after reviewing the documentation provided by the company. Therefore, the inspectors should finally recommend whether an inspection in a third country is necessary to fulfill the objectives of the requested inspection.