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Annual Report of the Pharmacovigilance Inspectors Working Group for 2010

Adopted by the PhV IWG on 24 March 2011

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1. Introduction

This document is the third Annual Report of the PhV IWG[1]. The Pharmacovigilance Inspectors Working Group (PhV IWG) has been established by the EMA, within the scope of article 57(1)(i) of Regulation (EC) No. 726/2004. Following a report on the first year of operation, the PhV IWG Mandate was endorsed by the Heads of Medicines Agencies on 18-19 May 2009 and by the EMA Management Board on 1 October 2009, thereby formally establishing the PhV IWG.

The PhV IWG focuses on harmonisation and co-ordination of PhV related activities at Community level. The group's role and activities are described in more detail in its Workplan. The group supports the co-ordination of the provision of PhV inspection related advice and provides a link with other groups such as CHMP[2], CVMP[3], and PhVWP (H+V)[4].

This Annual Report is set out in line with the format and objectives of the 2010 Workplan.

2. Meetings

The plenary meetings, involving PhV inspectors dealing with human medicinal products and PhV inspectors dealing with veterinary medicinal products, were held on the following dates:

- 23 February 2010
- 08 June 2010
- 23 September 2010
- 30 November 2010

A joint meeting PhV IWG and PhV WP assessors and two subgroup meetings with some delegates from both groups met also this year (see section 6).

3. Inspections conducted in support of the centralised procedure

Development of Pharmacovigilance inspections relating to centralised products

According to Volume 9A and the guideline on monitoring of compliance with PhV regulatory obligations and PhV inspections of veterinary medicinal products in Volume 9B, the CHMP and CVMP, respectively, in conjunction with the Competent Authority of the Member State (MS) in whose territory the MAH's QPPV is located and applicable Pharmacovigilance and Inspectors' Working Parties, will determine a programme for inspection in relation to centrally authorised products (CAPs). These inspections will be prioritised based on the potential risk to public health, the nature of the products, extent of use, number of products that the MAH has on the EEA market and other risk factors.

[1] Pharmacovigilance Inspectors Working Group
[2] Committee for Medicinal Products for Human Use
[3] Committee for Medicinal Products for Veterinary Use
[4] Pharmacovigilance Working Party (Human + Veterinary)

The focus of these inspections is to determine whether the MAH has the personnel, systems and facilities in place to meet their regulatory PhV obligations for CAPs in the EEA. These inspections will be requested as system inspections with one or more specific products selected as examples, for which specific information can be traced and verified through the various processes. This shall provide a practical evidence for the functioning of the MAH's PhV system in the Community and their compliance with the regulatory requirements.

In general, it is anticipated that national inspection programmes will fulfil the need for the routine inspections of this programme and therefore it is expected that the inspection programme will be achieved mainly through the national programmes. However there will be situations where these inspections might be specifically requested by the CHMP or CVMP, as applicable, (e.g. global PhV sites in third countries). Targeted inspections are also reflected in this programme as they may replace the need for a routine inspection.

The results presented in Table 1 and 2 show the number of inspections requested in relation to the Human and Veterinary 2010 PhV inspection programmes, respectively, and split by the type of site inspected.

Table 1- Human PhV Inspections Requested in 2010 in the context of the programme for PhV inspection of companies with CAPs

	QPPV (MAH) site	**Global PhV site**	**QPPV Subcontractor site**	**Subcontractor /Licensing partner site**	**Affiliate site**	**Total**
CHMP Requested	3	1	0	0	0	4
National Inspection Programmes	23	0	10	0	0	33
Total	26	1	10	0	0	37

Table 2- Veterinary PhV Inspections Requested in 2010 in the context of the programme for PhV inspection of companies with CAPs

	QPPV (MAH) site	**Global PhV site**	**QPPV Subcontractor site**	**Subcontractor /Licensing partner site**	**Affiliate site**	**Total**
CVMP Requested	1	0	0	0	0	1
National Inspection Programmes	6	0	1	0	1	8
Total	7	0	1	0	1	9

*It should be noted that these totals are just a subset of the total number of PhV inspections conducted in 2010 in EU/EEA, which is approximately 201 inspections for human medicinal products and 44 inspections for veterinary medicinal products.

4. Harmonisation topics

4.1. Procedures and Guidance documents

The following documents, concerning human and veterinary medicinal products, have been finalised:

- Classification of PhV Inspection findings (to be used in the context of the CXMP requests) to facilitate the publication of anonymised information on the areas of concern identified during PhV inspections.

The following documents, concerning human and veterinary medicinal products, are under preparation and expected to be finalized in the second or third quarter 2011:

- Procedure on the Follow Up of PhV Inspections.
- Guideline on communication of scheduled PhV inspections and information sharing of inspection outcomes.
- Guideline on Document Retention and Record Keeping for PhV Inspections.
- Procedure on Coordination of post-approval PhV Inspections for the centralised procedure.
- Triggers and risk factors for selection of sites/prioritisation for PhV inspections: points to consider for assessors.
- Pre-submission instructions and template for the "Detailed description of the PhV system" (DDPS) document for veterinary medicinal products.

The following document concerning only veterinary medicinal products has been agreed and will be finalised in 2011:

- Assessors' checklist in relation to the DDPS document assessment.

4.2. Joint Inspections

All 4 PhV inspections requested by the CHMP in 2010 (see Table 1 in section 3) have been joint inspections involving more than one MS. There was one PhV inspection requested by the CVMP (see Table 2 in section 3) but this was not conducted as a joint inspection.

4.3. Training and development

The following training activities have taken place during this year:

- A Pharmacovigilance inspection training took place from 15th to 17th November 2010 in Antwerp. Key objective of the training was to build an understanding and interaction between assessors and inspectors. The training was organised by Belgium (human and veterinary) and supported by the programme committee (human side: Denmark, PEI-Germany, France; vet side: France and the UK). Inspectors and assessors of both, veterinary and human units of Member States (Austria, Belgium, Bulgaria, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Malta, The Netherlands, Norway, Poland, Portugal, Slovenia, Sweden, UK) as well as inspectors, assessors and experts from candidate

countries (Croatia, the Former Yugoslav Republic of Macedonia, Serbia, Turkey) participated. The following topics were discussed in the workshops:

- Conduct of inspection (Inspection planning; Different types of inspections and problems met during conduct of an inspection).
- Handling of safety information on clinical studies (Break out session Human).
- Detailed Description of the Pharmacovigilance System (Break out session Vet).
- Discussion on the current state of PhV inspections in Europe.
- Classification of findings: clinical studies.
- PSUR evaluation - how assessors and inspectors can work together to have better inspections (PSUR-RMP evaluation; Assessors view).
- Classification of findings related to PSUR-RMP evaluation.
- Quality Management System - Quality Control – Audits.
- Identification and grading of findings related to Quality Management Systems (QMS) / Quality Control (QC) / Audits.
- Database / software validation.
- Identification and grading of findings - Database / software validation.
- Signal Detection / Management (User's view; Regulators expectation with Respect to Signal Management Activities and the Corresponding QC and Audit Aspects).

- During the PhV Inspector Working Group meetings held in 2010, discussions on the following topics have taken place:
  - Development of peer review of case studies.
  - Sharing and discussion of inspection report findings.

- Several Delegates from the PhV IWG have attended the inspector-specific Eudravigilance Data Analysis System training on 29 November 2010 with the aim to learn to prepare reports from Eudravigilance to facilitate the preparation of the inspections.

5. Pharmacovigilance topics

A) In relation to medicinal products for human use

- The PhV IWG has prepared and is maintaining the 2010-2013 risk-based programme for routine pharmacovigilance inspections of MAHs connected with human centrally authorised products (CAPs).
- PhV inspectors have also provided recommendation to the PhV WP and PhV IWG in relation to PhV inspections or related assessment issues.

B) In relation to medicinal products for veterinary use

- The PhV IWG has prepared and is maintaining the 2010-2012 risk-based programme for routine pharmacovigilance inspections of MAHs connected with veterinary centrally authorised products (CAPs).

These programmes are not publicly available as they contain confidential information.

6. Liaison with other groups

Interaction with the CHMP PhV WP and CVMP PhV WP

- PhV IWG – PhV WP subgroup meetings were held on 18 March and 21 October 2010. The following main topics were discussed by the subgroup:
  - Procedure on the Follow Up of PhV Inspections.
  - Guideline on communication of scheduled PhV inspections and information sharing of inspection outcomes.
  - Triggers and risk factors for selection of sites/prioritisation for PhV inspections.

- A joint meeting with the PhV WP assessors took place on 7 June 2010. The following main topics were discussed with a perspective from both sides:
  - DDPS Assessment.
  - Change of Ownership of MAs and DDPS.
  - EVDAS – Eudravigilance Data Warehouse Analysis System – queries, reports.
  - Inspection Follow up.
  - Case studies.
  - Risk Management Plans.

Communication with the public and external bodies

- Delegates from the PhV IWG have participated and given presentations on behalf of the group in different European Conferences, covering different topics of public interest.
  - Joint DIA/EFGCP Pharmacovigilance Audit and Inspection Workshop on 01 October 2010.

For the details of the activities of the PhV IWG see the Workplan for 2011.