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Annual Report of the Pharmacovigilance Inspectors Working Group for 2009

Adopted by the PhV IWG on 23rd February 2010

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Table of contents

1. Introduction

This document is the second 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 has been 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 2009 Workplan.

2. Meetings

The plenary meetings of the PhV IWG were held in the following dates:

- 11 March 2009
- 16 June 2009
- 23 September 2009
- 08 December 2009

The March and September plenary meetings were joint meetings involving inspectors dealing with human medicinal products and inspectors dealing with veterinary medicinal products. The June and December meetings were only human.

The PhV IWG-PhV WP subgroup, involving inspectors and assessors from the human and veterinary side, was held on 24 November 2009.

3. Inspections conducted in support of the centralised procedure

Development of Pharmacovigilance inspections relating to centralised products

According to the 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.

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

[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)

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 2009 PhV inspection programmes, respectively, and split by the type of site inspected.

Table 1- Human PhV Inspections Requested in 2009 in the context of the programme for PhV inspection of companies with CAPs

	QQPV (MAH) site	Global PhV site	QPPV Subcontractor site	Subcontractor /Licensing partner site	Affiliate site	Total
CHMP Requested	5	3	0	2	1	11
National Inspection Programmes	3	0	0	0	0	3
Total	8	3	0	2	1	14*

Table 2- Veterinary PhV Inspections Requested in 2009 in the context of the programme for PhV inspection of companies with CAPs

	QQPV (MAH) site	Global PhV site	QPPV Subcontractor site	Subcontractor /Licensing partner site	Affiliate site	Total
CVMP Requested	3	0	0	0	0	3
National Inspection Programmes	0	0	0	0	0	0
Total	3	0	0	0	0	3*

*It should be noted that these totals are just a part of the total number of PhV inspections conducted in 2009 in EU/EEA, which is approximately 213 inspections for human medicinal products and 36 inspections for veterinary medicinal products.

4. Harmonisation topics

4.1. Procedures and Guidance documents

A) Procedures and guidance for PhV inspections for medicinal products for human use

The PhV IWG has finalized and published the following document:

- Procedure for the preparation of a risk-based programme for routine pharmacovigilance inspections of MAHs connected with human CAP products.

The following documents are under preparation and will be included in the 2010 Workplan of the group:

- Guideline on triggers and risk factors for selection of sites for PhV inspection and its revision as required.
- Guideline on communication of inspection findings and information sharing process after the completion of a PhV inspection.
- SOP on Coordination of post-approval PhV Inspections for the centralised procedure.
- Guideline on follow up and actions to be taken after the completion of a PhV Inspection.

B) Procedures and guidance for PhV inspections for medicinal products for veterinary use

The PhV IWG has finalized and published the following documents on the EMA external web site:

- Procedure for the preparation of a risk-based programme for routine pharmacovigilance inspections of MAHs connected with veterinary CAP products.
- Procedure for coordinating pharmacovigilance inspections requested by the CVMP.
- Procedure for conducting pharmacovigilance inspections requested by the CVMP.
- Procedure for reporting pharmacovigilance inspections requested by the CVMP.

The following documents are under preparation and will be included in the 2010 Workplan of the group:

- Guideline on triggers and risk factors for selection of sites for PhV inspection and its revision as required.
- Guideline on communication of inspection findings and information sharing process after the completion of a PhV inspection.
- SOP on Coordination of post-approval PhV Inspections for the centralised procedure.
- Guideline on follow up and actions to be taken after the completion of a PhV Inspection.

4.2. Joint Inspections

13 out of the 14 PhV inspections requested by the CHMP and the 3 PhV inspections requested by the CVMP (see Table 1 and 2 in section 2) have been joint inspections involving more than one MS.

4.3. Training and development

The following activities have taken place during this year:

- A Pharmacovigilance inspection training took place from 19th to 20th of November 2009 in Paris. Key objective of the training was to build on understanding and interaction between assessors and inspectors. The training was organised by France (human and veterinary) and supported by the programme committee (Denmark, Germany/PEI (Human and Veterinary), Sweden and United Kingdom (Human and Veterinary). 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, Turkey) and from USA participated. The following topics were discussed in workshops:
  - Key aspects of PhV Inspection (subcontracting and marketing partners, QM system for PhV activities, regulated computer systems used for handling safety data and data of interest for pharmacovigilance activities, EU QPPV, processing of adverse events, reporting to competent authorities and to EMA, interaction between safety issues and product defects – batch recall, review of adeverse events by inspectors, training, PSUR process, safety surveillance process in clinical trials, ongoing monitoring process and updating of reference safety information)
  - PhV inspectors working group activities
  - EudraVigilance activities
  - Risk Management Plan Implementation
  - E2B Clinical Safety Data Management: Data Elements for Transmission of Individual Case Safety reports
  - Detailed Description of the Pharmacovigilance System assessment
  - New EU Pharmacovigilance Regulation
  - Non-EU pharmacovigilance regulations (USA, Japan)
- During the PhV Inspector Working Group meetings held in 2009, discussions on the following topics have taken place:
  - Development of peer review of case studies.
  - Sharing and discussion of inspection report findings.

5. Pharmacovigilance topics

A) In relation to medicinal products for human use

The PhV IWG has prepared and is maintaining the 2009-2012 programme on PhV inspections which is not publicly available as it contains confidential information:

- 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 2009-2011 programme on PhV inspections, which is not publicly available as it contains confidential information:

- Risk-based programme for routine pharmacovigilance inspections of MAHs connected with human centrally authorised products (CAPs)

The following documents are under preparation and will be included in the 2010 Workplan of the group:

- Pre-submission instructions and template for the "Detailed description of the PhV systems" (DDPS) document for veterinary medicinal products.
- Assessors' checklist in relation to the DDPS document assessment.

C) In relation to both, human and veterinary medicinal products

Documents on the following are under preparation and will be included in the 2010 Workplan of the group:

- Develop the processes for sharing information (what, when, how and what to do with it) in support of the inspection process and programme and for interaction between PhV inspectors and assessors and promote inspections via increased communication.
- Support the development of guidelines for the assessment of the "Detailed description of the PhV systems" (DDPS) that is submitted in Marketing Authorization Applications and suggest the relative input of assessors and inspectors to this process.

6. Collaboration with the European Commission

- The PhV IWG through the PhV IWG - PhV WP subgroup has contributed to the Detailed Variation Classification Guideline in relation to the classification of variation for the Detailed description of the PhV system.

7. Liaison with other groups

CHMP, CVMP and respective PhV WPs

- A PhV IWG – PhV WP subgroup meeting was held on 24 November 2009. The following main topics were discussed by the subgroup:
  - Post-inspection follow up. Development of processes and procedure on the actions to be taken after the completion of a PhV inspection.
  - Preparation of a procedure on triggers and risk factors for selection of sites for PhV inspections
- PhV Inspectors have provided recommendations to the PhV WP (human and veterinary) and attended the PhV WP meetings when needed to explain and discuss inspections findings and further recommendations.

Heads of Medicines Agencies (HMAs)

- The 2009 Annual report with the activities of the group was provided to the May 2009 HMA.
- The PhV IWG is an established group following the endorsement of its mandate by the Heads of Medicines Agencies on 18-19 May 2009 and by the EMA Management Board on 1 October 2009.

Other Regulatory Agencies

- An Expert from US FDA participated in the PhV inspectors training course held in Paris (see section 4.3).

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.

For the details of the activities of the PhV IWG see the Workplan for 2010.