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Annual Report of the Pharmacovigilance Inspectors Working Group for 2012

Adopted by the PhV IWG on 21 March 2013

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Table of contents

1. Introduction

This document is the fifth Annual Report of the Pharmacovigilance Inspectors Working Group (PhV IWG). The PhV IWG[1] 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 pharmacovigilance related activities at European Union 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 pharmacovigilance inspection related advice and provides a link with other groups such as CHMP[2], CVMP[3], PRAC (H)[4] and PhV WP (V)[5].

This Annual Report is set out in line with the format and objectives of the 2012 Workplan.

2. Meetings

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

- 21-22 March 2012;
- 24-25 May 2012;
- 03-04 October 2012;
- 13-14 December 2012.

Due to the implementation of the new human pharmacovigilance legislation, the meetings were organised to accommodate a joint session and two separate sessions, one dedicated to human and one to veterinary medicinal products only.

In addition, approximately monthly meetings (remote access was provided to attendees) of the Audits/Inspections project team for the implementation of the new pharmacovigilance legislation, including PhV IWG and PhV WP delegates (PRAC delegates since July 2012) were organised to discuss draft documents and specific topics, in particular items to support the implementation of the new pharmacovigilance legislation (see section 6).

3. Inspections conducted in support of the centralised procedure

Development of pharmacovigilance inspections relating to centralised products

For human medicinal products the CHMP with input from the Pharmacovigilance Risk Assessment Committee (PRAC) and in conjunction with the Competent Authority of the Member State (MS) in whose territory the pharmacovigilance system master file is located (Supervisory Authority) and the Inspectors' Working Group, have determined and maintain a programme for inspection in relation to

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

centrally authorised products (CAPs), in accordance with GVP Module III on Pharmacovigilance inspections.

For veterinary medicinal products, according to Volume 9B, Guidelines on pharmacovigilance regulatory obligations and pharmacovigilance inspections of veterinary medicinal products, the CVMP supported by the Pharmacovigilance Working Party, in conjunction with the Competent Authority of the Member State (MS) in whose territory the MAH's QPPV is located and the Inspectors' Working Group, have determined and maintain a programme for inspection in relation to centrally authorised products (CAPs).

The inspections in those programmes are 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 pharmacovigilance obligations for CAPs in the EEA. These inspections are 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 provides a practical evidence for the functioning of the MAH's pharmacovigilance system in the European Union 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 is achieved mainly through the national programmes. However there are situations where these inspections might be specifically requested by the CHMP or CVMP, as applicable, (e.g. global pharmacovigilance sites in third countries). For cause 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 2012 pharmacovigilance inspection programmes, respectively, and split by the type of site inspected.

Table 1- Human pharmacovigilance inspections requested in 2012 in the context of the programme for pharmacovigilance inspection of companies with CAPs

	QPPV (MAH) site	Global PhV site	QPPV Subcontractor site	Subcontractor /Licensing partner site	Affiliate site	Total
CHMP Requested	7	2	0	0	0	9**
National Inspection Programmes	24	0	1	1	0	26
Total	31	2	1	1	0	35*

Table 2- Veterinary pharmacovigilance inspections requested in 2012 in the context of the programme for pharmacovigilance inspection of companies with CAPs

	QPPV (MAH) site	Global PhV site	QPPV Subcontractor site	Subcontractor /Licensing partner site	Affiliate site	Total
CVMP Requested	2	0	0	0	0	2
National Inspection Programmes	5	0	0	0	0	5
Total	7	0	0	0	0	7*

* It should be noted that these totals are just a subset of the total number of pharmacovigilance inspections conducted in 2012 in EU/EEA, which is approximately 207 inspections for human medicinal products and 59 inspections for veterinary medicinal products.

** One of the site inspections was requested by the CHMP in 2012 but will be conducted in 2013.

4. Harmonisation topics

4.1. Implementation of the new human pharmacovigilance legislation

In relation to the implementation of the new human pharmacovigilance legislation the group contributed to the preparation and finalisation of the following Good Vigilance Practice Guideline modules:

- GVP Module I - Pharmacovigilance Systems and their Quality Systems;
- GVP Module II - Pharmacovigilance System Master File;
- GVP Module III – Pharmacovigilance Inspections;
- GVP Module IV - Pharmacovigilance System Audits.

In addition, the group contributed to the preparation of Q&A(s) and other guidance documents and specific guidance on the use of EMA databases and IT systems in relation to the pharmacovigilance system master file location, the contact details of the qualified person responsible for pharmacovigilance and inspection information sharing. The group also initiated the work for the preparation of the Union procedures on the planning, coordination, conduct, reporting, follow-up, sharing of inspection information and documentation of pharmacovigilance inspections, to support further harmonisation for the mutual recognition of pharmacovigilance inspections within the EU. The work on the implementation of the new pharmacovigilance legislation is ongoing.

4.2. Procedures and Guidance documents

The following documents, concerning human medicinal products, have been finalised in 2012:

- Distant/Virtual pharmacovigilance inspections of MAHs during a crisis situation – Points to consider.

The following document concerning veterinary medicinal products have been finalised in 2012:

- Record-keeping and archiving of documents obtained or resulting from the pharmacovigilance inspections.
- Recommendations on the training and experience of inspectors performing pharmacovigilance inspections.

4.3. Joint Inspections

The total of CHMP requested inspections in 2012 is nine. From the pharmacovigilance inspections requested by the CHMP and conducted in 2012/2013, six have been joint inspections involving more than one MS (see Table 1 in section 3). The two pharmacovigilance inspections requested by the CVMP (see Table 2 in section 3) were conducted as joint inspections.

4.4. Training and development

- A pharmacovigilance inspection training took place in Copenhagen, Denmark from 11th to13th of April 2012.The training was organised by the Danish Medicines Agency (human and veterinary), under the Danish Presidency, supported by the programme committee (Belgium, Denmark, France, Germany (PEI and BfArM) and the United Kingdom). 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, Ireland, Italy, Latvia, Lithuania, Malta, The Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain, Sweden, United Kingdom) as well as inspectors, assessors / experts from candidate countries (Croatia) and from third countries (Canada, Japan, Saudi Arabia, USA) participated. Key objectives of the training were:
  - to promote awareness and better understanding of new legislation and/or guidance, as applicable, with focus to the new pharmacovigilance legislation in relation to human medicinal products and to volume 9B in relation to veterinary medicinal products);
  - to share experiences from inspections (human and veterinary) conducted by individual member states in order to promote further harmonisation of inspection approaches;
  - to build an understanding and interaction between assessors and inspectors.
- The following topics were presented and/or discussed in the workshops:
  - Discussion on the current status of PhV inspections in Europe;
  - Presentation and discussion on anonymised inspection findings and their classification from different member states;
  - Training of Inspectors: Member states training policies - use of PIC/S and/or other joint inspection training/observational programme;
  - How do member states organize interactions between inspectors and assessors, with focus on interactions between assessors and inspectors when preparing and/or triggering inspections and in the follow up of pharmacovigilance inspections;
  - Quality management system - National procedures (SOPs) for pharmacovigilance inspections;
  - Use of EudraVigilance data Analysis System (EVDAS) by pharmacovigilance inspectors of MAHs of human medicinal products / EV DAS queries available;
  - Eudravigilance-Veterinary Data WareHouse (EV-Vet DWH): queries useful for inspectors/assessors of veterinary medicinal products and practical examples where information from EV-Vet DWH has been used for inspection;
  - Line listings and what to check for in Periodic Safety Update Reports (PSURs);
  - Computerised systems in pharmacovigilance amd IT/computer validation;

- Special requirements and considerations for vaccines and blood products;
- Topics on the new EU pharmacovigilance legislation (human medicinal products) – with focus on the main changes, transitional measures and impact on inspection processes;
- Detailed Description of the Pharmacovigilance System (DDPS) assessment (Vet);
- MedDRA (human medicinal products) and VeDRA (veterinary medicinal products) structure and coding from an inspector's viewpoint. What should inspectors look for in preparation of and during inspections;
- EudraVigilance (EV) and Data Analysis System (EVDAS) training of pharmacovigilance inspectors of human medicinal products took place on the 14November 2012;
- A EudraVigilance (EV) and Data WareHouse (DWH) workshop of pharmacovigilance inspectors of veterinary medicinal products took place on the 13 December 2012;
- Training sessions on the Good Vigilance Practices guidance for human medicinal products were introduced, as part of the PhV IWG plenary meetings with focus on the topics of interest for the group.

- During the PhV IWG meetings held in 2012, discussions on the following topics have taken place:
  - Development of peer review of case studies;
  - Sharing and discussion of inspection report findings;
  - EudraVigilance and Eudravigilance Data Analysis System demonstration of queries available to pharmacovigilance inspectors of veterinary medicinal products to facilitate the preparation of inspections.

5. Pharmacovigilance topics

A) In relation to medicinal products for human use

- The PhV IWG has prepared and is maintaining the 2012-2015 risk-based programme for routine pharmacovigilance inspections of MAHs connected with human centrally authorised products (CAPs).
- Pharmacovigilance inspectors have also provided recommendation(s) to the PhV WP, the PRAC from July 2012 and PhV IWG in relation to pharmacovigilance inspections or related assessment issues.

B) In relation to medicinal products for veterinary use

- The PhV IWG has prepared and is maintaining the 2012-2014 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 Pharmacovigilance Working Party and the Pharmacovigilance Risk Assessment Committee (PRAC) as of July 2012

- Sessions for PhV IWG – Assessors interaction were organised during the plenary meetings of PRAC (02 October 2012) and the PhV IWG (25 May 2012) to discuss topics related to the implementation of the new human pharmacovigilance legislation. The following main topics were discussed:
  - Interaction between Inspectors and assessors;
  - Marketing Authorisation conditions in relation to the existence of an adequate pharmacovigilance system.
- Approximately monthly meetings (remote access provided to attendees) of the Audits/Inspections project team for the implementation of the new pharmacovigilance legislation, including PhV IWG and PhV WP delegates (PRAC delegates since July 2012) were organised to discuss draft documents and specific topics, in particular items to support the implementation of the new pharmacovigilance legislation (see section 2 and section 4.1).

Interaction with the CVMP Pharmacovigilance Working Party

- The PhV IWG interacted with assessors on topics related to:
  - The Detailed Description of the Pharmacovigilance System (DDPS) document;
  - Follow up of pharmacovigilance inspections;
  - Training of assessors and inspectors;
  - Preparation and maintenance of the risk-based programme for routine pharmacovigilance inspections of MAHs connected with veterinary centrally authorised products (CAPs).

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.
  - Fourth (27/02/2012) stakeholder forum on the implementation of the new pharmacovigilance legislation;
  - Fifth (25/05/2012) stakeholder forum on the implementation of the new pharmacovigilance legislation;
  - Sixth (08/11/2012) stakeholder forum on the implementation of the new pharmacovigilance legislation;
  - Eudravigilance information day (05/10/2012).

For the details of the activities of the PhV IWG see the Workplan for 2013.