EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Compliance and Inspection

Mandate, objectives and rules of procedure for the Pharmacovigilance Inspectors Working Group

1. General considerations

The Pharmacovigilance Inspectors Working Group (PhV IWG) has been established by the European Medicines Agency (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.

Prior to the establishment of the PhV IWG, the Good Clinical Practice Inspectors Working Group (GCP IWG) dedicated one additional day from two of their regular quarterly meetings to the discussion of pharmacovigilance (PhV) inspection issues (i.e. one day each in September 2006 and February and September 2007). With the introduction of the revised pharmaceutical legislation and increasing use of pharmacovigilance inspection by regulators the inspectors recommended that a working group dedicated to pharmacovigilance inspection should be set up. A proposal for the establishment of an ad hoc Pharmacovigilance Inspectors Working Group for a preliminary period of one year was endorsed by the Heads of Medicines Agencies in January 2008, and agreed by the EMA Management Board in April 2008.

For human medicinal products, **Good Pharmacovigilance Practices** (GVP) and in particular GVP Module III on pharmacovigilance inspections (replacing the set of guidelines in Volume 9A of the Rules Governing Medicinal Products in the EU) clearly describe the pharmacovigilance inspection process and the involvement of the inspectors' group in the following sections:

III.B.5. Inspection process

> *"Pharmacovigilance inspections should be planned, coordinated, conducted, reported on, followed-up and documented in accordance with inspection procedures consistent with agreed Union pharmacovigilance inspection procedures developed by the PhV IWG to support harmonisation for the mutual recognition of pharmacovigilance inspections within the EU."*

III.B.10. Quality management of pharmacovigilance inspection process

> *"Quality and consistency of the inspections is facilitated by the Union procedures for pharmacovigilance inspections developed by the PhV IWG to support the mutual recognition of inspections within the EU mentioned in III.B.5."*

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III.C.3.1. General considerations

> *"Pharmacovigilance inspections should be planned, coordinated, conducted, reported on, followed-up and documented in accordance with inspection procedures consistent with agreed Union pharmacovigilance inspection procedures developed by the PhV IWG to support harmonisation for the mutual recognition of pharmacovigilance inspections within the EU as mentioned in section III.B.5."*

III.C.2.1. General role of the Agency

> *"As part of this coordination role the Agency is responsible for:*
>
> > *establishing and maintaining processes through the PhV IWG to support the consistency and quality of pharmacovigilance inspections of marketing authorisation holders with centrally authorised products conducted by inspectorates of the national competent authorities;"*

III.C.3.3. Inspection programmes

> *"A programme for routine inspections for centrally authorised products will be determined by the Agency in conjunction with the supervisory authorities of the Member States, the PhV IWG, the PRAC and the CHMP.*

For veterinary medicinal products, Volume 9B of The Rules Governing Medicinal Products in the European Union (guidelines on pharmacovigilance for medicinal products for veterinary use) describes the pharmacovigilance inspection process and clearly indicates the involvement of the inspectors' group in the following sections:

2.5.2

> *"The CVMP in conjunction with the NCA referred to in section 2.5.1 and the CVMP PhVWP-V and the applicable inspectors' working party, will determine a programme for inspection in relation to CAPs."*

2.5.11

> *"The Agency will establish procedures for the administration and review of inspection requests and reports in conjunction with the CVMP, PhVWP-V and relevant inspectors' working party.*

2.5.12

> *"Procedures for pharmacovigilance inspection will be prepared in association with pharmacovigilance inspectors and representatives of the PhVWP-V and will be updated as needed. These procedures will be adopted and published in line with the policies and procedures of the Agency on such documents."*

Thus, the PhV IWG will address all matters related directly or indirectly to pharmacovigilance inspections and carry out the tasks described under section 2. The key to its role is the development and implementation of procedures and processes to ensure harmonisation and mutual recognition, within the EU, of a high standard of pharmacovigilance inspection and harmonisation with the wider membership of the group.

The group will address inspection related pharmacovigilance issues in conjunction with the Pharmacovigilance Risk Assessment Committee (for human medicinal products) and the Pharmacovigilance Working Party (for veterinary medicinal products).

2. Mandate and objective

The PhV IWG provides input and recommendations on all matters relating directly or indirectly to the preparation, conduct and follow up of pharmacovigilance inspections in the context of post-

authorisation processes and irrespective of the marketing authorisation procedure. Its main goals are to promote an effective management of pharmacovigilance inspections in the Union, to establish proficient communication and information exchange and to provide input into pharmacovigilance legislation preparation.

Co-operation with the European Commission

- Discussions on practical implementation of pharmacovigilance guidelines, common interpretation of guidelines and harmonisation of pharmacovigilance inspection approaches in the EEA;
- Development, implementation and monitoring of plans for implementation/operation of MRAs and other similar Union arrangements, if applicable;
- Formulating advice and comment on issues related or having an impact on pharmacovigilance inspections including draft legislation to the European Commission.

Co-operation with EMA

- Providing advice to and liaising with the human Pharmacovigilance Risk Assessment Committee (PRAC) and Veterinary Pharmacovigilance Working Party (V-PhV WP) for the development of implementing texts for pharmacovigilance on matters relating to inspections;
- Development and agreement by consensus of pharmacovigilance inspections related guidelines for submission to the Agency's Executive Director for adoption;
- Development, agreement by consensus and maintenance of high-level procedures for the conduct of pharmacovigilance inspections as set out in GVP Module III on pharmacovigilance inspections and section 2.5 of Volume 9B of The Rules Governing Medicinal Products in the European Union for human and veterinary products respectively, dealing with topics including the selection of sites for inspection, the coordination, preparation, conduct and reporting of inspections as well as their follow-up. Agreed procedures will be submitted for adoption by the Agency's Executive Director;
- Development and agreement by consensus of other documents within the framework of pharmacovigilance guidelines and related documents in connection with inspections such as Reflection Papers and Questions and Answers to be published on the EMA website.
- Advising on and developing procedures for the coordination of inspections requested by the Scientific Committees – these procedures are published by the EMA;
- Formulating advice and comment on pharmacovigilance related issues to the scientific committees and their working parties;
- Liaison with Good Clinical Practice Inspectors Working Group, Good Manufacturing Practice Inspectors Working Group, CHMP and Pharmacovigilance Risk Assessment Committee (PRAC) for human medicinal products, CVMP and Veterinary Pharmacovigilance Working Party (V-PhV WP) for veterinary medicinal products, and other EMA or scientific committee working parties as applicable on matters of mutual interest.

Co-operation with Heads of Medicines Agencies (HMAs)

- When requested, formulating advice and comment on pharmacoviglance inspections related issues to HMA and its working groups;
- When requested, formulating advice and comment on pharmacovigilance inspections related issues to the Coordination Groups for Mutual Recognition and De-centralised Procedures (CMD h&v);
- Contribution to the development of the Benchmarking of European Medicines Agencies with respect to those elements related to pharmacovigilance inspections;
- Liaison and co-operation with the Working Group of Enforcement Officers (WGEO) on specific issues.

Training

- To promote and actively contribute to training of inspectors and the development of harmonised procedures and practices through training programmes and joint inspections;
- Increase shared experience through review of (anonymous) inspection reports and findings. Discussion of problem issues/case reports.

Co-operation with other bodies

- Liaison and cooperation on matters of mutual interest with international bodies. In particular: The World Health Organisation (WHO), the Pharmaceutical Inspection Cooperation Scheme (PIC/S), the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) and Veterinary Use (VICH) as well as Mutual Recognition Agreement (MRA) partners and key regulatory authorities;
- Liaison with interested parties (EFPIA, EuropaBio, EGA, AESGP, ISPE, ISOP, IFAH-Europe, EGGVP and other specific interested groups).

Communication with the public and external bodies

The PhV IWG will regularly communicate details of its work to external organisations and the general public using appropriate vehicles including in particular the EMA and HMA websites. Appropriate opportunities will be taken through international training courses and conferences to communicate on pharmacovigilance inspections.

3. Composition and rules of participation

Chairmanship

Meetings will be chaired by a representative of EMA inspection sector or delegate. Members may request, for specific topics coming under the heading of cooperation with HMA that a co-chair is appointed from within the members. Appointment of the co-chair will be by consensus of the members or, if necessary, using the voting rules described in section VI.4.

Membership

Membership is composed of experts nominated by the relevant national authority for human and/or veterinary medicinal products with senior responsibility and broad experience in the area of pharmacoviglance inspections. A replacement delegate, who would participate in those exceptional cases where the nominated member is unable to attend the meeting, may also be nominated.

Meeting documentation will be distributed by EMA to all members and any nominated replacements.

There will be one member from each of the EEA Member States with one additional member from each Member State where there is a separate pharmacovigilance inspectorate for human and for veterinary medicinal products. Members from EU Member States will be reimbursed for attendance at meetings. Additional staff of the authorities may attend with the chairman's agreement, in particular where their participation is needed for a specific topic. The European Commission – Directorate General of Public Health and Consumer Affairs (DG SANCO) will also be invited to send a representative to meetings.

The Executive Director of the Agency and members of EMA secretariat may attend all meetings.

Observers

Observers may include the representatives of EU accession countries.

Specific confidentiality rules will apply to observers. Observers attend at the discretion of the chairman, in line with EMA policy on observers, and may not be involved when particular items of concern to EU/EEA member states are discussed, product specific matters or other confidential matters.

Observers are encouraged to participate freely in discussions but shall not take part in any decision-making process.

Other observers may participate with the agreement of the chairperson in consultation with the group where possible, in line with EMA policy on observers.

4. Meeting frequency

The PhV IWG shall meet at least four times per year. Additional meetings may be held when planned for specific reasons such as training. The dates of the meetings shall be included in the work plan. Some meetings or parts of the meetings may involve joint activities with other working groups. Drafting groups will conduct the majority of their business by correspondence and teleconference but upon reasoned request meetings will be organised by EMA usually in the margins of the plenary meeting of the PhV IWG.

5. Duration of activity

Not applicable.

6. Rules of procedure

Responsibilities of chairperson

The chairperson is responsible for the efficient conduct of the business of the PhV IWG and shall in particular:

- plan the work of the PhV IWG;
- monitor that the rules of procedure are respected;
- ensure that at the beginning of each meeting that any potential conflict of interest is declared regarding any particular item to be discussed;
- aim to achieve consensus on issues discussed;
- decide in exceptional cases, when a vote is necessary;
- ensure, the regulatory and scientific consistency of recommendations;
- co-ordinate the work of PhV IWG with that of the Agency's scientific committees, working parties and other relevant groups of EMA, the Heads of Medicines Agencies or the European Commission;
- report on the activities of PhV IWG to the Agency's scientific committees, working parties and other relevant groups of EMA, the Heads of Medicines Agencies or the European Commission as appropriate.

Responsibilities of EMA secretariat

The EMA secretariat shall provide technical, scientific, legal, regulatory and administrative support to the PhV IWG. This includes the following:

- prepare for and co-ordinate the work of the PhV IWG;
- organise meetings and ensure timely circulation of meeting documents;
- facilitate the necessary contacts between the PhV IWG and other bodies;
- ensure adequate co-ordination of the work carried out by the PhV IWG and other concerned groups;
- contribute to the overall quality assurance and assurance of scientific and regulatory consistency of the documents/recommendations of the PhV IWG;
- prepare the agenda, table of actions and summary records of meetings;
- communicate, in a pro-active manner, any output of the PhV IWG to the interested parties;
- transmit any recommendations of the PhV IWG to the relevant body for adoption and/or publication as appropriate.

Responsibilities of members

Membership implies a commitment to actively participate in the work of the PhV IWG and to regularly attend the meetings.

- Members shall ensure that they communicate the views of the Member State, which they represent when contributing to discussions and decisions.
- Members shall ensure that all agreements are communicated within their Member State and should ensure that necessary steps are taken to act upon decisions as appropriate.
- Members may identify and propose topics for consideration by the PhV IWG. Any proposal should be supported by a problem statement or other adequate justification.
- Members tabling documents for discussion at meetings of the PhV IWG shall respect the guidelines prepared by the group for this purpose or the relevant Union guidelines.
- Members shall observe deadlines for the submission of documents to EMA to allow for timely distribution of documents to other members in order to enable them to establish the position of the Member State that they represent.

Organisation of meetings

- The meetings will be held and meeting minutes prepared in English.
- The draft agenda for every meeting shall be circulated, together with the relating documents, by the EMA Secretariat, in consultation with the chairperson, at least 14 calendar days before the meeting.
- When a Member of the PhV IWG is unable to participate in a meeting or a part of the meeting, or in a discussion topic due to a conflict of interest, he/she must inform the Secretariat in writing in advance.
- The PhV IWG shall prepare and agree an annual work plan. The work plan shall be reviewed regularly and updated as necessary.
- A quorum is required for all decisions or recommendations of the PhV IWG. This shall be reached when two thirds of the total members of the PhV IWG are present.
- Whenever possible, decisions or recommendations of the group shall be taken by consensus. If such a consensus cannot be reached, the chair or any member may propose a vote. Each Member State shall have 1 (one) vote. An absolute majority (i.e. favourable votes by at least half of the total number of members eligible to vote plus one) will be required. Divergent positions shall be mentioned in the summary record of the meeting.
- Prior to any vote the group will agree, depending on the nature of the topic, whether any members should not participate in the vote.

Drafting groups

When further consideration is required in order to prepare proposals on specific topics drafting groups may be convened constituted of members of the PhV IWG or other experts, as appropriate.

The drafting group will report to the PhV IWG.

Rules of procedure for drafting groups will be developed.

Guarantees of independence

The members of the PhV IWG and experts referred to above shall not have any direct interests in the pharmaceutical industry that could affect their impartiality. They shall undertake to act in the public interest and in an independent manner, and shall make an annual declaration of their financial interests. All indirect interests, which could relate to the pharmaceutical industry, shall be entered in a register held by the Agency, which is accessible to the public, on request at the Agency's office.

Members and experts attending meetings shall declare at the beginning of each meeting any specific interests, which could be considered to be prejudicial to their independence with respect to the points of the agenda. These declarations shall be made available to the public.

The specific provisions for handling declarations of interests and confidentiality undertakings as defined in the EMA Policy on the handling of conflicts of interests of scientific committee members and experts (EMA/513078/2010) and the EMA breach of trust procedure (EMA/154320/2012) are applicable to members of the PhV IWG and experts participating in the activities of the PhV IWG.

Code of conduct

Members of the PhV IWG and experts participating in EMA's activities shall abide by the principles set out in the EMA Code of conduct.

Contacts with interested parties

- Where relevant, the PhV IWG will establish contacts, on an advisory basis, with parties concerned with the manufacture and control of medicinal products.
- The pharmaceutical industry, health care professionals, patients/consumers or other interested parties have the opportunity to comment in writing on draft guidelines and general regulatory developments during the public consultation of the documents.
- When considered appropriate by the PhV IWG, oral or written presentations by interested parties can be made during meetings at earlier stages of development of the guidelines. The PhV IWG may also meet with interested parties to discuss general matters or specific issues.
- In any case, the PhV IWG shall neither conduct any deliberations nor reach any formal decisions in the presence of members of interested parties.
- Before any consultation session, interested party representatives and the PhV IWG members will communicate to the EMA secretariat points they would like to discuss, so that a session agenda can be prepared for agreement by chairperson and circulation by EMA secretariat.

General provisions

Members of the PhV IWG as well as the observers and all experts shall be bound, even after the cessation of their duties, not to disclose any information, which, by its nature, must be covered by individual professional secrecy. When participating in international or other forums on behalf of the PhV

IWG, members shall ensure that the views expressed are those of the PhV IWG. When participating in international or other forums not specifically on behalf of the PhV IWG, members shall make clear that the views expressed are their own views, or those of the national competent authority, independent of the views of the PhV IWG.