European Medicines Agency

23 June 2005
Doc. Ref. EMEA/CHMP/PhVWP/88786/04

MANDATE, OBJECTIVES AND RULES OF PROCEDURE FOR THE CHMP PHARMACOVIGILANCE WORKING PARTY

(ADOPTED BY THE PHVWP ON 21 JUNE 2005 AND THE CHMP ON 23 JUNE 2005)

I. GENERAL CONSIDERATIONS

According to its Rules of Procedure, the Committee for Medicinal Products for Human Use (CHMP) may consult its Working Parties on any scientific issue related to their specific fields of expertise. The CHMP may also delegate certain tasks associated with the scientific evaluation of applications, or drafting of guidelines to the relevant Working Parties. The tasks identified by the CHMP should be included in the work programme of each Working Party to be adopted by the CHMP.

The CHMP Pharmacovigilance Working Party (PhVWP) is therefore established to provide recommendations to the CHMP on all matters relating directly or indirectly to pharmacovigilance and to perform the tasks described under section II. Upon request of National Competent Authorities (NCAs), the PhVWP provides recommendations for non-centrally authorised products. This dual reporting line justifies the deviation in some aspects of the Mandate and Rules of Procedure of the PhVWP compared with other CHMP Working Parties.

The PhVWP was already established in 1995 under the previous Committee, the CPMP. A revised mandate was adopted by the CPMP and the Heads of Medicines Agencies in 2003. This revised mandate is incorporated in this document, which provides in addition the Rules of Procedure.

II. MANDATE AND OBJECTIVES

II.1 Mission and Responsibilities

The mission of the PhVWP is to provide advice on the safety of medicinal products authorised in the European Union (EU) and the investigation of adverse reactions to enable effective identification, assessment and management of risk, at any phase in the product life cycle. On the basis of such advice the PhVWP will provide, where applicable, recommendations for regulatory action to its stakeholders, i.e. the CHMP/EMEA and NCAs. The advice given should be in a precise and operational format and in accordance with timeframes set by such stakeholders taking into account the needs of the stakeholders as defined, where applicable, in Community legislation.

This should enable effective management and subsequent communication of risk. Best use of pharmacovigilance resources available in the EU will have to be considered when trying to achieve the above objectives. Effective utilisation of tools for information exchange will have to be applied in order to improve the access to and utilisation of pharmacovigilance information.

The key responsibilities of the PhVWP are:

- Evaluation of potential signals arising from spontaneous reporting, including those identified from the EudraVigilance database, and all other sources, including epidemiological databases, studies and published literature;
- Provision of advice on confirmation and quantification of risk and on regulatory options;

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 86 68
E-mail: mail@emea.eu.int http://www.emea.eu.int
©EMEA 2005 Reproduction and/or distribution of this document is authorised for non-commercial purposes only provided the EMEA is acknowledged

- Risk management by advising on risk management plans;
- Monitoring regulatory action and the outcomes of such action;
- Setting standards for procedures and methodologies to promote good vigilance practice;
- Promotion of communication and exchange of information between the EMEA and NCAs;
- International cooperation.

II. 2 Deliverables of the PhVWP to the CHMP

II.2.1 Centralised Procedures

II.2.1.1 Pre-Authorisation Phase

The PhVWP will, when requested by the CHMP, provide support to the CHMP by peer reviewing, in accordance with a set timeframe, the report(s) prepared by the specialised expert(s), appointed by the CHMP to reply to the questions raised by the CHMP on pre-clinical issues with a potential impact on the post-authorisation phase, and on clinical safety issues. Situations for which involvement of the PhVWP may be required will be decided by the CHMP on a case-by-case basis.

II.2.1.2 Post-Authorisation Phase

The PhVWP will

- either (Scenario 1: involvement of the PhVWP, when requested by the Rapporteur) address the questions put to the PhVWP and propose to the CHMP recommendations for regulatory action;
- or (Scenario 2: involvement of specialised expertise, in addition to the involvement of the PhVWP, when requested by the Rapporteur) peer review the report prepared by the Rapporteur's PhVWP representative, including the replies provided by the specialised expert(s) to the questions put to such expert(s) and propose to the CHMP recommendations for regulatory action. The PhVWP can also identify the need for specialised expertise involvement.

Situations for which involvement of the PhVWP may be required, depending on the impact on the risk-benefit balance of the medicinal product are:

- Follow-up of safety related issues already considered by the PhVWP in the pre-authorisation phase;
- Follow-up of risk management plans agreed upon by the CHMP during the adoption of the Opinion on the initial application for marketing authorisation;
- Follow-up of post-authorisation safety studies;
- Safety signals of potential public health impact which need to be confirmed or quantified;
- Confirmed or quantified safety signals;
- Safety issues which could lead to a substantial change to the use of the medicinal product or medical practise.

II.2.2 Referral Procedures

The same arrangements as stated for the handling of product related issues for centrally authorised products (post-authorisation phase, section II.2.2.2 above) will apply. Situations for which involvement of the PhVWP may be required will depend on the scope of the referral procedure and the questions raised by the CHMP.

II.2.3 Interaction with the CHMP

- The agenda items relating to the CHMP deliverables will be prepared in consultation with the CHMP. The full PhVWP agenda will be sent to the CHMP for information.
- Any item, requested by the CHMP to be discussed by the PhVWP, should, in addition to a written CHMP request, preferably also be introduced to the PhVWP orally by the CHMP Member in charge of the issue at CHMP level, in liaison with the respective PhVWP Member.
- An oral report on the outcome of the PhVWP meetings will be provided to the CHMP by the PhVWP Chairperson.

©EMEA 2005

- More specifically, on the items discussed by the PhVWP at the request of the CHMP, the final outcome should be provided in writing and presented orally to the CHMP by the PhVWP Member in charge together with the respective CHMP Member, for in-depth discussion by the CHMP as needed.
- The minutes of PhVWP meetings are sent to the CHMP for information.

II. 3 Deliverables of the PhVWP to National Competent Authorities

II.3.1 Pre-Authorisation Phase

The PhVWP will, when requested by the (future) Reference Member State (RMS), provide support by advising on the report(s) prepared by the RMS or specialised expert(s), appointed by the RMS, on the questions raised on pre-clinical issues with potential impact on the post-authorisation phase, and on clinical safety issues. The PhVWP will give advice on the risk management plan in accordance with a set timeframe.
Other situations for which involvement of the PhVWP may be required will be decided on a case-by-case basis by the NCAs.

II.3.2 Post-Authorisation Phase

a) The PhVWP will review the assessment of potential safety signals arising from spontaneous reporting, including those identified from the EudraVigilance database, and from all other sources (e.g. periodic safety update reports, literature, epidemiological studies), either
   - on the basis of a report submitted by the RMS or any Member State which should allow the PhVWP to confirm and quantify the risk. A timetable and action plan for assessment should be defined, or
   - systematically, whenever possible, a RMS or any Member State is considering a formal referral for safety reasons (the national position should be clearly explained and the proposed question(s) identified).

b) The PhVWP will review the assessment and advise on regulatory options or make recommendations on the basis of the report provided by the RMS or any Member State.
   - If needed the RMS or any Member State will propose the inclusion of specialist expertise (from their own NCA or other NCAs).
   - The assessment report should be accompanied by a draft advice to the NCAs with recommendations for mechanism and timing of implementation and communication.
   - Such advice may include a risk management plan.
   - There should be adequate time for consideration by NCAs prior to formal advice by the PhVWP.
   - Where possible, the goal should be a single PhVWP discussion leading to advice formally agreed by the PhVWP.

c) The follow-up of previous PhVWP advice will be based on agreed
   - Criteria for revisiting the discussion;
   - Monitoring of action on recommendations and implementation of changes to Summaries of Product Characteristics by NCAs.

   Moreover, the following situations may need the involvement of the PhVWP:
   - Follow-up of safety related issues already considered by the RMS or the PhVWP in the pre-authorisation phase;
   - Follow-up of risk management plans;
   - Follow-up of post-authorisation safety studies;
   - Follow-up of safety related issues identified in the EudraVigilance database.

©EMEA 2005

II.3.3 Interaction between the PhVWP and National Competent Authorities

II.3.3.1 Interaction with Heads of Medicines Agencies

The PhVWP will give advice to the Heads of Medicines Agencies on implementation of recommendations. Such advice will also address the communication strategy and documents.
Where relevant, the PhVWP will prepare a report which summarises the main advice on the issues discussed for which the assessment has been finalised, together with proposals for action. Such report will be communicated to the Heads of Medicines Agencies.

II.3.3.2 Interactions with the Mutual Recognition Facilitation Group (MRFG)1

- The agenda of the PhVWP will be sent to the MRFG for information.
- The minutes of the PhVWP will be provided to the MRFG.

II.3.3.3 Communication and exchange of information

The PhVWP will develop tools in order to promote the communication and exchange of information between the NCAs and the EMEA, and to track the implementation of recommendations.

II. 4 Deliverables of the PhVWP to both the CHMP and National Competent Authorities

II.4.1 Standard Setting by the PhVWP

The PhVWP is involved in the development of principles, procedures and guidelines for regulators and pharmaceutical industry:

- Development of common principles and procedures on the different elements of the European Risk Management Strategy, for agreement by the CHMP/EMEA/European Commission and the NCAs;
- Development and revision of European guidance documents for regulatory authorities and pharmaceutical industry at the request of the CHMP/EMEA/European Commission and the NCAs;
- Contribution to the process of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH);
- Contribution to the preparation and revision of Community legislation, at the request of the European Commission.

II.4.2 International Co-operation between the PhVWP and Regulatory Authorities/Health Institutions

II.4.2.1 Co-operation with the US Food and Drug Administration (FDA)

At the request of the EMEA's Management Board Working Group on Costing on 18 March 1999, the PhVWP discussed principles of possible cooperation and coordination with the FDA and agreed with the FDA to hold regular teleconferences.
The aim of such teleconferences is to identify or confirm safety signals, to inform about available pharmacovigilance data and the outcome of their assessment as well as to alert each other of possible upcoming regulatory action in relation to pharmacovigilance issues.
The interaction between the PhVWP and the FDA has to comply with the terms of the Confidentiality Arrangements concluded between the EU and the FDA for centrally processed applications and arbitration/referral procedures. For non-centrally authorised products, the cooperation between the PhVWP and the FDA is still under discussion.

[1] In November 2005, the MRFG will be replaced by the Coordination Group set up in accordance with Article 27 of Directive 2001/83/EC of the European Parliament and of the Council as amended by Directive 2004/27/EC.

©EMEA 2005

II.4.2.2 Co-operation with the World Health Organization (WHO)

In accordance with Article 27 of Council Regulation (EC) No. 726/2004 the EMEA shall collaborate with the WHO on international pharmacovigilance and shall submit promptly to the WHO appropriate and adequate information regarding the measures taken in the EU related to the marketing authorisations of centrally authorised products which may have a bearing on public health protection in third countries. Such legal obligation for co-operation has been translated into the document "Principles of Providing the World Health Organization with Pharmacovigilance Information" (Volume 9 of the Rules Governing Medicinal Products in the European Union, Human Medicines). Such principles also elaborate on the collaboration between Member States and the WHO for non-centrally authorised products.

III. COMPOSITION AND RULES OF PARTICIPATION

III.1 Composition

a) The PhVWP is composed of experts selected from the European experts list according to their specific expertise.

b) The PhVWP will consist of 1 representative per Member State (PhVWP Members). The representatives will be appointed by the NCAs. Relevant information on such representatives is included in the EMEA's database of the European experts list. The EMEA will reimburse travel and accommodation expenses for 1 representative per Member State and for the Chairperson of the PhVWP.
   - Additional experts may attend the meetings of the PhVWP. Relevant information on such experts will be entered in the EMEA's database.
   - Members who want to bring additional experts should notify the EMEA Secretariat in advance of the meeting, subject to the agreement of the Chairperson.
   - Representatives of Iceland, Liechtenstein and Norway are invited to attend the meetings of the PhVWP (non-voting PhVWP Members, they may not be elected Chairperson nor Vice-Chairperson).
   - Observers from Accession Countries may have standing invitations to participate in the meetings of the PhVWP.
   - Observers from other non-EEA Countries may participate with the agreement of the Chairperson and the EMEA.

III.2 Rules of Participation

Membership of the PhVWP implies a commitment to participate actively in its work and to attend its meetings regularly. A Member may nominate a replacement to participate in those exceptional cases where he or she is unable to attend a meeting.

Meeting documentation will be distributed to an agreed list of recipients drawn up by the EMEA with the agreement of the Chairperson.

CHMP Members are encouraged to take an active role in the activities of the PhVWP.

IV. MEETING FREQUENCY

The PhVWP shall meet 11 times per year. Meetings of the PhVWP will be held in parallel with the meetings of the CHMP in order to allow interaction between PhVWP representatives and the CHMP. The dates of the meetings shall be included in the PhVWP work programme. In urgent situations an extraordinary meeting can be organised. The organisation of meetings is subject to the availability of the necessary funds.

©EMEA 2005

V. DURATION OF ACTIVITY (IN THE CASE OF TEMPORARY WORKING PARTIES)

Not applicable, as the PhVWP is a standing Working Party.

VI. RULES OF PROCEDURE

VI.1 Responsibilities of Chairperson and Vice-Chairperson

a) The Chairperson and, in his/her absence, the Vice-Chairperson is responsible for the efficient conduct of the business of the PhVWP and shall in particular:
   - plan the work of the PhVWP together with the EMEA Secretariat;
   - monitor, together with the EMEA Secretariat, that the Rules of Procedure are respected;
   - ensure that at the beginning of each meeting any potential conflict of interest is declared regarding any particular item to be discussed by the PhVWP;
   - aim to achieve consensus on issues discussed by the PhVWP;
   - decide in exceptional cases, when a vote is necessary;
   - ensure, together with the PhVWP and the Secretariat, the regulatory and scientific consistency of the PhVWP's recommendations;
   - co-ordinate together with the EMEA Secretariat the work of the PhVWP with that of the other relevant Working Parties of the EMEA;
   - report on the activities of the PhVWP to the CHMP or other Working Parties as appropriate;
   - may call upon ad hoc or regular support in their duties from PhVWP Members or other regularly attending experts according to need and expertise.

b) The Vice-Chairperson will deputise for the Chairperson when the latter is unable to chair either all or part of the PhVWP meeting. On such occasions the Chairperson will seek the agreement of the Vice-Chairperson as early as possible, prior to the meeting, and the EMEA Secretariat shall be informed immediately.

VI.2 Election of Chairperson and Vice-Chairperson

The Chairperson of the PhVWP is appointed by the CHMP for the term of the Committee and such appointment may be renewed. CHMP Members, their alternates or Members of the PhVWP may be elected by the CHMP to fulfil the responsibilities. Regardless of the time of election of the Chairperson he/she shall be appointed for the term of the CHMP.

The PhVWP shall appoint a Vice-Chairperson. The Vice-Chairperson should be appointed amongst the PhVWP Members.

Nominations should be submitted in writing to the EMEA Secretariat no later than the start of the CHMP meeting at which election of the PhVWP Chairperson is to take place. Candidates shall submit a brief résumé in support of their candidature at the time of the nomination.

The election of the Chairperson shall follow the same procedure as that for the election of the Chairperson of the CHMP as stated in Article 3, paragraphs 1 to 4, of the Rules of Procedure of the CHMP, adapted accordingly to the PhVWP Members. The election of the Vice-Chairperson will be carried out by the PhVWP (this has been delegated by the NCAs) and will follow the same principles as for the election of the Chairperson.

VI.3 Organisation of Meetings and Reporting Arrangements

VI.3.1 Organisation of PhVWP Meetings

a) The PhVWP shall meet at the EMEA. The Secretariat of the PhVWP is provided by the EMEA.

b) The meetings will normally be of 3 days duration.

©EMEA 2005

c) The meetings will be held and minuted in English, without interpretation.

d) The draft agenda for each meeting shall be circulated, together with the relevant documents, by the EMEA Secretariat, in consultation with the Chairperson, at least 14 calendar days before the meeting.

e) The running order of the meetings should be organised in a manner allowing interaction with the CHMP as outlined under II.2.3.

f) When a Member of the PhVWP is unable to participate in a meeting, part of a meeting, or discussion topic due to conflict of interest, he/she must inform the Secretariat in advance in writing.

g) The PhVWP may identify and propose topics on non-product related issues for its consideration. Any proposal for a guideline providing adequate justification shall be transmitted to the CHMP for endorsement and shall be preceded by a concept paper to be endorsed by the CHMP.

h) Recommendations from the PhVWP on centrally authorised products or products subject to a referral procedure shall be transmitted to the CHMP for adoption. Product-specific reports for the CHMP should be prepared by the PhVWP Member representing the Rapporteur based on the summary from the assessment report with the addition of the PhVWP discussion and conclusion and, where relevant, specialised expert input.

i) Recommendations agreed by the PhVWP on products that are authorised nationally or through mutual recognition should be transmitted both to the Heads of Medicines Agencies and the MRFG.

j) When considered appropriate by the PhVWP, oral presentations by companies can be made during the PhVWP meetings on matters directly related to the activities of the PhVWP. For centrally authorised products or products subject to a Referral procedure such oral presentations are subject to agreement of the CHMP.

k) The PhVWP shall prepare an annual work programme for adoption by the CHMP, which shall include topics identified by the PhVWP and any specific tasks/topics identified by the CHMP. The work programme shall be regularly reviewed and updated as necessary with the agreement of the CHMP.

l) The Chairperson will be invited to attend plenary CHMP meetings to report on the activities of the PhVWP and ensure liaison with the work of the CHMP.

m) The mandate of the PhVWP shall be agreed by the CHMP and Heads of Medicines Agencies. It shall be reviewed, at least at the start of each new term of the CHMP.

VI.3.2 Organisation of Teleconferences between the PhVWP and the FDA

a) Teleconferences between the PhVWP and the FDA will be held in the margins of the PhVWP meetings.

b) The frequency of such teleconferences will be agreed between the PhVWP, the EMEA and the FDA.

c) A separate agenda will be prepared for such teleconferences and agreed between the PhVWP, the EMEA and the FDA in advance of the meetings.

d) Such teleconferences may be attended by the PhVWP Chair and the PhVWP Members (Member State representatives as well as representatives from Iceland, Liechtenstein and Norway), representatives of the European Commission and the EMEA.

©EMEA 2005

VI.4 Drafting Groups

When further consideration is required in order to prepare proposals on specific topics, the PhVWP may convene drafting groups constituted of Members of the PhVWP or other experts, as appropriate. The organisation of such meetings is subject to available funds. The drafting group will report directly to the PhVWP.

VI.5 Participation of Experts in Meetings

a) When necessary, the PhVWP may avail itself of the services of experts in specific scientific or technical fields. Such experts shall have proven experience in the assessment of medicinal products or in their field of expertise and be included in the European experts list. Where appropriate, Members from patient organisations, healthcare professional organisations or learned societies may act as experts.

b) In the context of the procedure for the "Handling of Safety Concerns for Pre- and Post-Authorisation Applications Processed in Accordance with the Centralised Procedure" (EMEA/CPMP/4285/04), specialised expertise for risk management might be required at the PhVWP. The involvement of such experts should follow the procedure for the handling of safety concerns above and any related organisational document prepared by the EMEA.

c) The names of any experts participating in PhVWP meetings shall be notified to the EMEA Secretariat before the meeting which they are due to attend.

VI.6 Guarantees of Independence

a) The Members of the PhVWP and experts referred to above shall not have any direct interests in the pharmaceutical industry, which 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 that could relate to the pharmaceutical industry shall be entered in a register held by the EMEA, which is accessible to the public on request at the EMEA's premises.

b) Members of the PhVWP and experts attending their 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 on the agenda. These declarations shall be made available to the public.

c) The specific provisions for handling declaration of interests and confidentiality undertakings as defined in the "EMEA Policy on the Handling of Conflicts of Interests for CHMP Members and Experts" (EMEA/H/31653), adopted by the EMEA Management Board, are applicable to Members of the PhVWP and experts participating in the activities of the PhVWP.

VI.7 Code of Conduct

Members of the PhVWP and experts participating in the EMEA's activities shall abide by the principles set out in the EMEA Code of Conduct.

VI.8 EMEA Secretariat

a) Under the authority of the Executive Director, the EMEA Secretariat shall provide support to the PhVWP. This includes the following:
   - provide technical and scientific support to Rapporteurs (guidelines), and other Members of the PhVWP;
   - provide legal, regulatory and scientific support to the PhVWP;
   - prepare and co-ordinate the work of the PhVWP in consultation with the Chairperson/Vice-Chairperson;

©EMEA 2005

- prepare the agenda in consultation with the Chairperson/Vice-Chairperson;
- ensure, if appropriate, that the periods laid down by Community legislation are complied with;
- organise meetings of the PhVWP ensuring timely circulation of meeting documents;
- facilitate the necessary contacts between the PhVWP and the CHMP;
- ensure adequate co-ordination of the work carried out within the PhVWP, the CHMP and other concerned working parties and/or scientific advisory groups;
- contribute to the overall quality assurance and assurance of scientific and regulatory consistency of the documents / recommendations of the PhVWP in co-operation with the Chairperson or Vice-Chairperson, as appropriate, taking into account the dual reporting line at the PhVWP;
- prepare the minutes of the meetings of PhVWP in consultation with the Chairperson/Vice-Chair;
- communicate when necessary any CHMP recommendations relevant to the PhVWP to interested parties;
- contribute to the identification of experts;
- prepare a table of conclusions for circulation after the meeting.

b) The Executive Director of the EMEA, members of the EMEA Secretariat, Members of the CHMP and representatives of the Commission, may attend all meetings of the PhVWP.

VI.9 Contacts with Interested Parties

a) Co-operation with interested parties, including the scientific community, will be notified to the CHMP and undertaken as considered appropriate, depending on the issue being raised. In particular, such contacts will be established, on an advisory basis, with parties concerned with the use of medicinal products, in particular patient organisations and healthcare professional organisations.

b) Pharmaceutical industry, healthcare 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.

c) When considered appropriate by the PhVWP, oral presentations by interested parties may be made during PhVWP meetings in earlier stages of development of guidelines. The PhVWP may also meet with interested parties to discuss general matters or specific scientific issues with the agreement of the CHMP and under specific conditions to be agreed by the CHMP.

d) In any case, the PhVWP shall neither conduct any deliberations, nor reach any formal decisions in the presence of representatives of interested parties.

e) Before any consultation session, interested party representatives and the PhVWP Members will communicate to the EMEA Secretariat the points they would like to be discussed, so that an agenda of the session can be prepared for agreement by the PhVWP Chairperson and circulation by the EMEA Secretariat.

VI.10 General Provisions

The Members of the PhVWP as well as 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. Specific confidentiality rules will apply to observers.

When participating in international or other fora not specifically on behalf of the CHMP, PhVWP Members shall make clear that the views expressed are their own views and not those of the CHMP.

©EMEA 2005