European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

EMEA/CHMP/SAWP/69686/04 Rev 6

MANDATE, OBJECTIVES AND RULES OF PROCEDURE OF THE SCIENTIFIC ADVICE WORKING PARTY (SAWP)

I GENERAL CONSIDERATIONS

Having regard to Article 56(3) of European Parliament and Council Regulation (EC) 726/2004, which provides that *"The Executive Director, in close consultation with the Committee for Medicinal Products for Human Use and the Committee for Medicinal Products for Veterinary Use, shall set up the administrative structures and procedures allowing the development of advice for undertakings, as referred to in Article 57(1)(n), particularly regarding the development of new therapies. Each committee shall establish a standing working party with the sole remit of providing scientific advice to undertakings."*

Having regard to Preamble (25): *"The field of activity of the Scientific Committees should be enlarged and their operating methods and composition modernised. Scientific advice for future applicants seeking marketing authorisation should be provided more generally and in greater depth. Similarly, structures allowing the development of advice for companies, in particular, small and medium-sized enterprises should be put in place ..."*

Having regard to Article 57(1) of European Parliament and Council Regulation (EC) 726/2004, which provides that *"the Agency, acting particularly through its committees, shall undertake the following tasks: (n) advising undertakings on the conduct of the various tests and trials necessary to demonstrate the quality, safety and efficacy of medicinal products";*

Having regard to Article 58(1) and (2) of European Parliament and Council Regulation (EC) 726/2004 which provides that

- *(1) "The Agency may give a scientific opinion, in the context of cooperation with the World Health Organisation, for the evaluation of certain medicinal products for human use intended exclusively for markets outside the Community. For this purpose, an application shall be submitted to the Agency in accordance with the provisions of Article 6. The Committee for Medicinal Products for Human Use, may, after consulting the World Health Organisation, draw up a scientific opinion in accordance with Articles 6 to 9. The provision of Article 10 shall not apply".*
- *(2) "The said Committee shall establish specific procedural rules for the implementation of paragraph 1, as well as for the provision of scientific advice."*

Having regard to Article 78(2) of European Parliament and Council Regulation (EC) 726/2004 which provides that *"The committees referred to in Article 56(1) and any working parties and scientific advisory groups established in accordance with that Article shall in general matters establish contacts, on an advisory basis, with parties concerned with the use of medicinal products, in particular patient organisations and health-care professionals' associations. Rapporteurs appointed by these committees may, on an advisory basis, establish contacts with representatives of patient organisations and health-care professionals' associations relevant to the indication of the medicinal product concerned."*

Having regard to Article 6 of the Regulation (EC) No. 141/2000 *"The sponsor of an orphan medicinal product may, prior to the submission of an application for marketing authorisation, request advice from the Agency on the conduct of the various tests and trials necessary to demonstrate the quality,*

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safety and efficacy of the medicinal product, in accordance with [Article 51 (j) of Regulation (EEC) No 2309/93, as amended[1]].”

The Committee for Medicinal Products for Human Use (CHMP) and the Committee for Orphan Medicinal Products (COMP) establish the Scientific Advice Working Party (SAWP) as a standing working party with the sole remit of providing scientific advice and protocol assistance to Applicants[2].

II OBJECTIVES AND MANDATE

As a main objective, the Scientific Advice Working Party shall provide scientific advice for medicinal products for human use and Protocol assistance for orphan medicinal products to facilitate access of medicinal products to patients and users of medicines by optimising Research and Development, reducing uncertainties in regulatory outcomes, and accelerating time for (to?) approval of a Marketing Authorisation Application. The SAWP shall therefore encourage Applicants to engage, as early as possible, in an ongoing dialogue with the Agency on the development of their product. The European Medicines Agency shall establish the best possible environment for the provision of scientific advice and protocol assistance, ensuring through its Scientific Committees flexibility towards Applicants and consistency between Scientific Advice and Protocol Assistance given to Applicants.

In view of the above:

1. The SAWP shall bring forward an integrated view as regards quality, pre-clinical and clinical safety including pharmacovigilance and risk/minimisation aspects, and efficacy, relating to the development of medicinal products and orphan medicinal products to the CHMP for adoption within a defined timeframe and format. This also includes follow-up advice given with a view to optimise the development of medicinal products and orphan medicinal products.

2. When applicable, the SAWP shall provide protocol assistance as regards demonstration of significant benefit relating to orphan medicinal products, and bring its view forward to the COMP for adoption within a defined timeframe and format.

3. The SAWP shall provide broader and more general advice for specific types of medicinal products or treatments.

4. The SAWP shall provide scientific advice to support the qualification of innovative drug development methods (e.g. use on a novel biomarker (BM) as an acceptable technical standard for a specific intended use in the context of pharmaceutical R&D. This qualification process, leads to the provision of either
    a. CHMP Scientific Advice of further development plans for the method to be performed for qualification purposes, based on the evaluation of the scientific rationale and on preliminary data submitted, or
    b. CHMP Qualification Advice on the acceptability of a specific use of the proposed method based on final assessment of data submitted.

5. The SAWP shall provide advice about the justification on whether a specific medicinal product being developed for a specific therapeutic indication falls within one of the categories set out in Article 2 and fulfils the condition laid down in Article 4(1)(c) of Commission Regulation (EC) No 507/2006 of 29 March 2006 on the conditional marketing authorisation for medicinal products for human use, which are defined in Article 14(7) of Regulation (EC) No 726/2004.

6. The SAWP shall provide advice on the acceptability of the development programme for conditional marketing authorisations, which are defined in Article 14(7) of Regulation (EC) No 726/2004

[1] Article 51 (j) of Regulation (EEC) No 2309/93, as amended corresponds to article 57(1)(n) of Parliament and Council Regulation (EC) 726/2004

[2] Throughout the document the term Applicant is used and encompasses Sponsors, Companies, Enterprises, Research institutes and WHO.

7. The SAWP shall provide advice about the justification for applying for a marketing authorisation under exceptional circumstances (Guideline on procedures for the granting of a marketing authorisation under exceptional circumstances, pursuant to article 14(8) of Regulation (EC) No 726/2004; EMEA/357981/2005)

8. The SAWP shall provide advice on the acceptability of the development programme for marketing authorisation application under exceptional circumstances, pursuant to article 14(8) of Regulation (EC) No 726/2004.

9. The SAWP shall provide advice on the design of trials to assess safety and efficacy in a new indication expected to bring significant clinical benefit compared to existing therapies as defined in Article 14(11) of Regulation (EC) No 726/2004 or Article 10(1) fourth subparagraph of Directive 2001/83/EC.

10. The SAWP shall provide advice on the design of trials to assess safety and efficacy in a new indication for a well-established substance in accordance with Article 10(5) of Directive 2001/83/EC as amended as by Directive 2004/27/EC.

11. The SAWP shall provide scientific advice for products intended for marketing outside the Community, in the context of co-operation with the WHO.

12. The SAWP shall provide advice on paediatric developments.

13. The SAWP shall pay special attention to development and methodology issues of products intended for small populations and adaptive designs in late stage drug development.

14. The SAWP shall take into account the specific needs of small and medium-sized enterprises (SMEs).

15. The SAWP shall provide advice for products intended for the new mandatory centralised procedure, i.e. acquired immune deficiency syndrome, cancer, neurodegenerative disorders, diabetes and, as of 20 May 2008, autoimmune diseases and other immune dysfunctions and viral diseases.

16. The SAWP shall provide scientific advice and protocol assistance and mobilise appropriate and specific expertise, especially for new and emerging therapies such as gene therapy and associated cell therapies, and xenogenic cell therapy and for questions related to pharmacogenetics/pharmacogenomics.

17. The SAWP shall establish contact with patients' organisations and health-care professionals' associations. Where appropriate, the SAWP shall consult them for the provision of Scientific Advice or Protocol Assistance.

18. The SAWP shall cooperate with the other EMEA Committees, Working Parties, Scientific Advisory Groups and the EMEA scientific secretariat, in particular to create a guideline document in a specific therapeutic area, publish standard Questions & Answers documents for frequently asked questions, and organise workshops and think-tank meetings on specific and rapidly evolving topics.

19. The SAWP shall ensure consistency between Scientific Advice and Protocol Assistance given to Applicants, available EU guidance documents and CHMP assessment.

20. The SAWP shall provide opportunities to Applicants to discuss with other regulatory agencies their global development programmes, in particular with the FDA. This should follow a request from the Applicant to the EMEA to arrange such parallel advice procedure.

21. The SAWP shall not be responsible for providing regulatory assistance for medicinal products and orphan medicinal products.

22. The SAWP shall not be responsible for advice prior to submission for qualification of a request for an accelerated assessment procedure [Guideline on the Procedure for Accelerated Assessment Pursuant to Article 14(9) of Regulation (EC) No 726/2004 (EMEA/419127/05)]

23. The SAWP shall not be responsible for Paediatric Investigational Plans as defined in the Regulation on medicines for children.

24. The SAWP shall not be responsible for pre-assessment of data that will be used to support future marketing authorisation applications**.**

25. The SAWP shall not be responsible for compassionate use as defined in Article 83 of Regulation (EC) No 726/2004

III RULES OF PROCEDURE

Composition

Article 1

1. The SAWP is a Multidisciplinary Expert Group and includes the Chairperson and 26 Members, among which 1 Vice-Chairperson and 3 COMP Members.

2. The SAWP includes at least the following expertise:
   - Pre-clinical safety: at least two representatives
   - Pharmacokinetics: at least one representative
   - Methodology and Statistics: at least two representatives.
   - Therapeutic fields for which there are frequent requests and/or defined in the annex of the new Regulation, e.g. cardiology, oncology, diabetes, neurodegenerative disorders, and infectious diseases including HIV infection.

3. The respective Chairperson of the Safety Working Party (SWP) and Efficacy Working Party (EWP) should be invited to each SAWP meeting.

4. The Chairperson of the CHMP can be invited to the SAWP meetings.

5. A senior statistician from the CHMP can be invited to the SAWP meetings.

6. At least one member of the SAWP will be part of each Qualification Team, the specialised group appointed by the CHMP for each individual qualification advice request.

Appointment of Chairperson, Vice-Chairperson and SAWP members

Article 2

1. The CHMP shall appoint 23 SAWP members for a term of three years renewable, upon proposals from CHMP members. These SAWP members may be CHMP members or European experts.

2. The COMP shall nominate 3 of its members for a term of 3 years renewable

In keeping with the CHMP rules of procedures:

3. The Chairperson of the SAWP shall be elected by the members of the CHMP for the term of the Committee, which may be renewed. A Committee member, an alternate or a member of the SAWP may be elected by the Committee to fulfil this responsibility. Where the

Chairperson does not belong to the CHMP, he/she shall be invited to attend plenary CHMP meetings to report on the activities on the SAWP and ensure liaison with the work of the CHMP. The Vice Chairperson of the SAWP shall be elected by the CHMP for the term of the Committee, which may be renewed.

4. Nominations should be submitted in writing to the EMEA secretariat no later than the start of the CHMP meeting at which election of SAWP chairpersons is to take place.

5. Candidates shall submit a brief résumé in support of their candidature at the time of the nomination.

6. The election of the Chairperson and the Vice-Chairperson shall be by absolute majority of the CHMP Members (i.e. favourable votes by at least half of the total number of CHMP members eligible to vote plus one) and by secret ballot. At each round, the candidate(s) with the lowest number of favourable votes shall withdraw. In the case of a tie in the decisive round, another round is organised with two remaining candidates. If, at the decisive round, the candidate with the highest number of votes does not get an absolute majority, a further voting is organised with this candidate only, where he/she needs favourable votes by at least half of the total number of Committee members eligible to vote plus one, to be elected Chairperson or Vice-Chairperson, as the case may be.

7. Each member of the SAWP referred to under Article 1(1) may have only one defined alternate.

Responsibilities of Chairperson and Vice-Chairperson

Article 3

1. The Chairperson shall be responsible for the efficient conduct of the business of the SAWP. The Chairperson has, in particular, the following responsibilities:
   - To ensure that the best possible advice is given.
   - To ensure consistency of advice given within the same therapeutic area;
   - To manage the business of the agenda by:
     - Ensuring all members have equal opportunity to express their views, taking into account time constraints
     - Formulating questions and proposals, summarising discussions, concluding on all items of discussions.
   - To endeavour to achieve consensus in the adoption of scientific advice and protocol assistance letters while taking into account other positions should a consensus not be reached;
   - To ensure that any potential conflicts of interest which have been declared to the secretariat are resolved before the particular item is discussed by the SAWP
   - To ensure that the rules of procedures are respected
   - To ensure that the co-ordinator's report is of the agreed format and of good quality.
   - To liaise regularly with the EMEA Secretariat to plan the work of the SAWP

2. When the Chairperson is not available to chair the meeting, the Vice-Chairperson shall take the chair.

Co-ordinators and Assessment Teams

Article 4

1. For any Scientific Advice or Protocol Assistance procedures, the Chair of the SAWP shall appoint two Co-ordinators. For any follow-up Scientific Advice or Protocol Assistance procedures, one the two Co-ordinators involved in the initial request will be appointed. For Protocol Assistance, if the request includes issues relating to demonstration of significant

benefit a third Co-ordinator (one of the three COMP representatives to the SAWP) shall be appointed by the Chair of the SAWP.

2. To be appointed as Co-ordinators, SAWP members shall provide the EMEA Secretariat with a notification of interest prior to the SAWP meeting. The Chair of the SAWP shall allocate the requests according to expertise and equal opportunity for each member. The appointment of scientific advice or protocol assistance co-ordinators is decided independently from any previous appointment of Rapporteurs/Co-Rapporteurs for centralised applications.

3. Each appointed SAWP Co-ordinator shall form their assessment team with external experts and/or internal assessors, which shall be notified to the EMEA before the start of the procedure.

   Appointed Co-ordinator(s) shall participate to EMEA presubmission meetings when these are requested by applicants.

4. The Co-ordinators are responsible for providing reports in response to the scientific advice or protocol assistance requests taking into account the procedure and timetable for evaluation of such requests. If necessary, the Co-ordinators may ask the Applicant for any additional documents or clarifications during the procedure. Should such contacts take place, these should be reported to the EMEA/SAWP.

5. The Co-ordinators shall compile questions and comments from the SAWP, the COMP (for protocol assistance), the Working Parties, Scientific Advisory Groups and the CHMP, where applicable.

6. The Co-ordinators shall draft the list of issues for the Discussion Meeting. The Discussion Meeting shall be chaired by one of the two Co-ordinator(s).

7. The provision of services by co-ordinators or their assessment teams shall be governed by written contract between the Agency and the person concerned, or where appropriate between the Agency and his/her employer. The person concerned, or his/her employer, shall be remunerated in accordance with a scale of fees to be included in the financial arrangements established by the Management Board.

8. The SAWP may consult relevant Working Parties or Scientific Advisory Groups in relation to the evaluation of preclinical and/or clinical questions including safety, for a specific product within the agreed timelines. The SAWP shall also delegate the task of evaluating quality related issues to the Biotechnology Working Party (BWP) or Quality Working Party (QWP). Situations where such consultation or delegation is done should be defined in a Standard Operating Procedure (SOP).
   In such cases, the Applicant's request and draft co-ordinator's report(s) shall be forwarded to the relevant working party or Scientific Advisory Group. If no working party or Scientific Advisory Group meeting are planned within the agreed timelines, a written consultation of the relevant working party or Scientific Advisory Group shall be carried out.
   In all situations, the Working Party or Scientific Advisory Group shall report to the SAWP. The SAWP remains responsible for the consolidated advice forwarded for adoption to the CHMP and COMP if applicable.

9. CHMP members are encouraged to take an active role in the activities of the SAWP.

Biomarker qualification team

Article 5

1. The Qualification Team is appointed based upon a proposal by the EMEA secretariat in conjunction with the CHMP and SAWP Chairs and led by a Coordinator who is a CHMP or SAWP member.

2. The Qualification Team shall consist of minimum 5 members and will be tailored to each individual qualification advice request. Resources will be derived from the CHMP, SAWP, working parties and the larger EU experts' network.

Involvement of Additional Expertise[3]

Article 6

1. The SAWP may involve additional expertise (including patients representatives if necessary) in Scientific Advice and Protocol Assistance for all aspects (pharmaceutical, preclinical, clinical and significant benefit). Additional expertise shall be consulted in particular for the provision of protocol assistance for orphan medicinal products.

2. Any SAWP member (including SAWP member not being a co-ordinator) or the EMEA may propose additional experts.

3. Additional expertise should be identified as early as possible and notified to the EMEA. The SAWP may appoint additional expertise to ensure the highest level of scientific knowledge in particular at the Discussion Meetings.

4. Additional expertise is regularly involved in the qualification of biomarkers.

Final scientific advice and protocol assistance letters

Article 7

1. Whenever possible, scientific advice and protocol assistance advice letter shall be adopted by consensus of appointed SAWP members. If such a consensus cannot be reached, scientific advice and protocol assistance advice letter shall reflect the position of the majority of SAWP members, while taking into account other positions. However, the final letter should indicate the preferred option. If less than 2/3 of the members (or alternates) are present, a written procedure shall be carried out.

2. Having regard to Directive 2001/20/EC, the SAWP may express ethical concerns on protocols submitted by Applicants. However, this position shall not substitute for the opinion of appropriate Ethics Committees.

3. The SAWP shall transmit their conclusions for Scientific Advice and Protocol Assistance to the CHMP and COMP (in case of issues on significant benefit) for formal adoption of the respective parts within a defined timeframe and format.

4. The final adopted advice letter, signed by the respective Chairpersons on behalf of the CHMP and the COMP (if applicable), shall be sent to Applicants following the CHMP/COMP meeting.

5. The Applicant may request a clarification after receipt of the final advice letter. This is only intended to provide the Applicant with the opportunity to comment on parts of the SA/PA that are not clear enough. The steps for requesting clarification after receipt of the final advice letter shall be defined in a Standard Operating Procedure.

6. CHMP scientific advice letters including advices on studies to be performed for biomarker qualification purpose are confidential (II4a). CHMP qualification advices on the acceptability of a specific use of the proposed method (II4b) are published for consultation before qualification.

[3] Additional expertise includes either experts not belonging to the National Authorities, or internal assessors not being part of the coordinators' assessment team, or both. Expertise is defined here by relevant work performed in the area, e.g. clinical practice, performance of studies or trials, publications.

Organisation of the meetings

Article 8

1. The SAWP shall meet monthly at the Agency. The meeting shall generally be held 2 weeks before the CHMP and its duration shall be 3 days. SAWP Members should endeavour to attend all meetings.

2. The dates of meetings are decided on an annual basis in consultation with the SAWP.

3. The meetings shall be held in English.

4. The draft agenda for every meeting shall be circulated together with the related documents by the EMEA Secretariat in consultation with the Chairperson at least 14 calendar days before the meeting.

5. When a Member of the SAWP is unable to participate to a meeting, he/she must inform the Secretariat in advance in writing and request his/her replacement by his/her appointed alternate.

Discussion meetings

Article 9

1. The SAWP may invite an Applicant to attend discussion meeting in connection with a scientific advice procedure. For Protocol assistance, the SAWP shall endeavour to organise discussion meetings. Discussion meetings shall also be organised where the SAWP does not agree with any important aspect of the programmes proposed by the Applicant or when no consensus within the SAWP members can be reached.

2. When the SAWP has delegated tasks associated with the evaluation of quality related issues, discussion meetings may be held with the Biotechnology Working Party (BWP) or Quality Working Party (QWP). Any additional issues should be systematically reported to the co-ordinators. Co-ordinators and the relevant experts of their assessment teams may attend the meeting.

3. When the need for a discussion meeting is agreed by the SAWP, the Co-ordinators and other SAWP members may nominate additional experts to participate in the Discussion Meeting. In addition, the meeting shall be open to all SAWP members.

4. A detailed list of issues to be addressed by the Applicant during the discussion meeting shall be adopted and sent to the Applicant following the SAWP meeting, together with the invitation and the meeting agenda. The Applicant shall be informed of the exact timing well ahead of the meeting.

5. The Applicant may also propose in writing additional points for discussion not part of the adopted list of issues. These additional points must be strictly related to the specific Scientific Advice/Protocol Assistance request submitted by the Applicant.

6. The discussion meeting shall be held in accordance with a Standard Operating Procedure.

Guarantees of independence

Article 10

1. SAWP Members, their alternates and experts shall not have financial or other 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. Any indirect interest connected with this industry must be declared promptly and recorded in a register held by the Agency, which the public may consult.

2. SAWP Members shall declare, at each meeting, any specific interests, which could be considered to be prejudicial to their independence with respect to the items on the agenda. These declarations shall be made available to the public.

3. SAWP Members and their experts shall abide by the principles set out in the EMEA Code of Conduct.

4. Specific provisions for handling declaration of interests and confidentiality as defined in the EMEA Policy on the Handling of Conflicts of Interests for Committee Members and Experts, adopted by the Managements Board (EMEA/H/31653) shall be applicable to SAWP members and experts participating in the SAWP activities.

5. SAWP Members shall not accept from the Member States any instructions incompatible with the tasks incumbent upon them within the Agency. It is essential for these tasks to remain strictly scientific in nature.

EMEA Secretariat

Article 11

Under the authority of the Executive Director, the EMEA Secretariat shall provide scientific, technical, and administrative support to the SAWP with a view to the performance of its duties and shall provide secretarial services to:

- Organise pre-submission and briefing meetings with Applicants and Co-ordinator(s)
- Prepare the work of the SAWP in consultation with the chairperson
- Ensure compliance with the timelines and procedures for the adoption of the final letters
- Forward convening papers, and all available documents at least 14 calendar days before the meeting of the SAWP
- Propose additional expertise including patients representatives if necessary
- Carry out the validation of the applications
- Facilitate the necessary contacts between the SAWP and the applicants
- Prepare the table of decision of the SAWP meetings
- Prepare the final letter for adoption by the SAWP/CHMP and COMP (when appropriate),
- Ensure adequate co-ordination of the work carried out within the SAWP
- Provide legal and regulatory support to the SAWP
- In the framework of the quality management and quality assurance of procedures, ensure consistency between advice given, guidelines and CHMP assessment within the same therapeutic area, and contribute to the peer review by SAWP, CHMP and EMEA of scientific advice/protocol assistance.
- Ensure that all relevant information is shared between COMP and CHMP
- Ensure that all relevant information from scientific advice and protocol assistance is included in the scientific advice database, which shall contribute to the scientific support brought about by EMEA both in terms of regulatory and scientific memory.

Approved by the Executive Director of the EMEA on 22 March 2006

Adopted by the CHMP on 31 May 2006

Entry into force: 1 July 2006