November 2014
EMA/151751/2010 Rev.3
Committee for Medicinal Products for Human Use (CHMP)

# Procedural Advice on CHMP/CAT/PRAC Rapporteur/Co-Rapporteur appointment principles, objective criteria and methodology in accordance with Article 62 (1) of Regulation (EC) No 726/2004

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| Adoption by CHMP | | September 2006 |
| Adoption by CAT/CHMP | Revision 1 | September 2009 |
| Adoption by CHMP | Revision 2 | March 2010 |
| Adoption by CAT/CHMP/PRAC | Revision 3 | November 2014 |

The key element of this revision is the inclusion of the appointment of PRAC Rapporteurs for centralised procedures, referrals, signals, PSURs.

Readability of the document has been enhanced through inclusion of information in tabular form and changes to the order of certain sections.

Finally reference is also made to relevant SOPs on the Methodology of the appointment of Rapporteur / Co-Rapporteur and their assessment teams, rather than including the detailed methodology in this document.

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# 1. Introduction

The **Committee for Medicinal Products for Human Use (CHMP)** is responsible for preparing the opinion of the Agency on any question relating to the evaluation of medicinal products for human use. Specifically the CHMP is responsible for the assessment of applications for marketing authorisation submitted under the centralised procedure as well as the assessment of referrals on human medicines (in the case of referrals related to pharmacovigilance issues, on the basis of the recommendation prepared by the PRAC).

The **Committee for Advanced Therapies (CAT)** is responsible for preparing the opinion of the Agency on any question relating to the assessment of advanced therapy medicinal products (ATMPs). Specifically, the CAT is responsible for the assessment and preparation of draft opinions on ATMP applications submitted under the centralised procedure.

The **Pharmacovigilance Risk Assessment Committee (PRAC)** is responsible for assessing all aspects of the risk management of medicines for human use. The main responsibility of the PRAC is to prepare recommendations on any questions relating to pharmacovigilance activities in respect of medicines for human use and on risk-management systems, including the monitoring of the effectiveness of those risk-management systems.

For any scientific evaluation in respect of a procedure submitted under the centralised procedure, a rapporteur and if relevant a co-rapporteur shall be appointed from amongst the members and alternates of the CHMP. For ATMPs, a rapporteur, and if relevant a co-rapporteur, shall be appointed from amongst the members and alternates of the CAT; in addition two CHMP co-ordinators will be appointed (one supporting the CAT rapporteur assessment team and another supporting the CAT co-rapporteur assessment team). In addition, for activities covering all aspects of the risk management of the use of human medicinal products, a rapporteur, and if relevant a co-rapporteur, shall be appointed from amongst the members and alternates of the PRAC.

For the evaluation of safety related referrals resulting from the evaluation of data relating to pharmacovigilance, a rapporteur, and if relevant a co-rapporteur, shall be appointed from amongst the members and alternates of the PRAC.

For the evaluation of all other referrals, a rapporteur, and if relevant a co-rapporteur, shall be appointed from amongst the members and alternates of the CHMP.

The appointment of rapporteur/co-rapporteur is made on the basis of objective criteria, which will ensure the provision of objective scientific opinions and will allow the use of the best and available expertise in the European Economic Area (EEA) on the relevant scientific area.

This paper outlines the principles, objective criteria and the procedure on the rapporteur/co-rapporteur appointment procedure.

# 2. Legal basis

The Pharmaceutical legislation Regulation (EC) No 726/2004, as amended by Regulation (EU) No 1027/2012 provides the legal framework for the rapporteur/co-rapporteur appointment.

> *Article 62(1) states "Where, in accordance with this Regulation, any of the committees referred to in Article 56(1) is required to evaluate a medicinal product for human use, it shall appoint one of its members to act as rapporteur, taking into account existing expertise in the Member State. The committee concerned may appoint a second member to act as co-rapporteur."*

*Article 61(1) states: "…The **alternates** shall represent and vote for the members in their absence and may act as rapporteurs in accordance with Article 62".*

*Note: For PRAC, in accordance with Article 61a(1), only those alternates appointed by the Member States may be appointed to act as rapporteurs*

*Article 57(1) states that the Agency [and therefore its Scientific committee(s) Members] shall provide the best possible scientific advice: "The Agency shall provide the Member States and the institutions of the Community with the best possible scientific advice on any question relating to the evaluation of the quality, safety and efficacy of medicinal products for human or veterinary use which is referred to it in accordance with the provisions of Community legislation relating to medicinal products."*

*In accordance with Article 61(5), the Members of the committee (and therefore the appointed Rapporteur/Co-Rapporteur) have the task in providing objective scientific opinions: "In addition to their task of providing objective scientific opinions to the Community and Member States on the questions which are referred to them, the members of each committee shall ensure that there is appropriate coordination between the tasks of the Agency and the work of competent national authorities, including the consultative bodies concerned with the marketing authorisation."*

*Article 61(6) states with regard to the scientific evaluation and resources: "Members of the committees and experts responsible for evaluating medicinal products shall rely on the scientific evaluation and resources available to national marketing authorisation bodies. Each competent national authority shall monitor the scientific level and independence of the evaluation carried out and facilitate the activities of nominated committee members and experts. Member States shall refrain from giving committee members and experts any instruction which is incompatible with their own individual tasks or with the tasks and responsibilities of the Agency."*

**For re-examinations of opinions under the centralised procedure**

- Article 62(1) (fourth sub-paragraph) of Regulation (EC) No 726/2004 of the European Parliament and of the Council
- Article 11 of the CHMP Rules of Procedure (EMEA/45110/2007)
- Article 10 of the CAT Rules of Procedure (EMEA/CAT/454446/2008)
- Article 11 of the PRAC Rules of Procedures (EMA/PRAC/488608/2012)

**For Similar Biological medicinal products**

- Article 10.4 of Directive 2001/83/EC, as amended
- Annex I to Directive 2001/83/EC, Part II, Section 4
- Notice To Applicants, Volume 2A, Chapter 1

**For referrals**

- Article 13 of Commission Regulation (EC) No 1234/2008
- Article 29 of Directive 2001/83/EC ("Mutual Recognition and decentralised referral")
- Article 29 of Regulation (EC) No 1901/2006

- Article 30 of Directive 2001/83/EC (“Harmonisation referral”)
- Article 31 of Directive 2001/83/EC (“Union interest referral”)
- Article 20 of Regulation (EC) No 726/2004 (“Referral for centrally authorised products only”)
- Article 5(3) of Regulation (EC) No 726/2004
- Article 107i of Directive 2001/83/EC (“Urgent Union procedure”)
- Notice to Applicants (NTA), Volume 2A, Chapter 3.

**Re-examination of a referral**

- Article 32 of Directive 2001/83/EC, as applicable

**For signals**

- Article 107h of Directive 2001/83/EC

**For Periodic Safety Update Reports (PSURs)**

- Article 107e of Directive 2001/83/EC for PSURs single assessment
- Article 28(3) of Regulation (EC) 726/2004 for PSURs for centrally authorised products

Committee specific documents also elaborate on the matter and clarify the roles and responsibilities of their members:

CHMP

- The CHMP Rules of Procedure (EMEA/45110/2007)
- The Notice to Applicants (Chapter 4)
- Procedural Advice to CHMP Members (EMEA/361945/2007)

CAT

- The CAT Rules of Procedure (EMEA/CAT/454446/2008)
- The procedural advice on the evaluation of ATMPs (EMEA/630043/2008)

PRAC

- The PRAC Rules of Procedure (EMA/PRAC/488608/2012)

# 3. Scope of this paper

This paper sets the principles, objective criteria and the methodology on the rapporteur/co-rapporteur appointment procedure.

These principles and objective criteria shall apply to several application types (e.g. centralised applications, applications under Article 58 of Regulation (EC) No 726/2004, compassionate use).

Additional principles are added for the rapporteur/co-rapporteur appointment for other types of application procedures; this includes Generics, Hybrids, re-examination of an opinion, signals and PSURs.

Similarly additional principles are added for the rapporteur/co-rapporteur appointment for referrals and re-examinations when applicable.

It should also be noted that the CHMP has established a peer review procedure. Such procedure foresees the appointment of peer reviewers during the initial phase of the assessment of new Marketing Authorisation Applications (MAAs). Such appointment is made on a voluntary basis. For ATMPs, there will be a peer reviewer coming from both CAT and CHMP.

In the post-authorisation phase, when a change in legal status is foreseen (e.g. switch from prescription to non-prescription), a peer reviewer shall be appointed to work with the existing Rapporteur and Co-Rapporteur already in place for the given medicinal product. The suitable candidate for peer review should have relevant knowledge of the area of non-prescription medicinal products and if possible previous experience in changing the legal status of a medicine/active substance from prescription to non-prescription.

# 4. Role of the rapporteur and co-rapporteur

The rapporteur and co-rapporteur for the CHMP/PRAC/CAT committees will:

- Take responsibility for the scientific assessment/evaluation undertaken by the assessment team within the scope of their committee's involvement with the concerned procedure in accordance to the timeframes laid down in the EU legislation and the EMA regulatory procedures
- Coordinate input from her/his assessment team
- Coordinate input from a variety of fora e.g. Working Parties, Ad Hoc Expert Groups, SAGs (Scientific Advisory Groups), external meetings/conferences
- Involve additional expertise as considered necessary
- Act as a committee representative/spokesman in liaison with Applicant/MAH
- Interact with the EMA product team
- Ensure that all her/his activities are performed in a transparent manner (informing accordingly the EMA Secretariat)
- Establish contacts with Patient Organisations/Health Care Professional Associations (in accordance with the provisions laid down in Article 78(2) of Regulation (EC) No 726/2004)
- Collaborate with the rapporteur from other relevant EMA committees for the medicinal product for human use and ensure comments are taken on board, as appropriate
- Conclude rapporteurship with the completion of required documentation as appropriate (Assessment Report, Draft Opinion etc.)

# 5. Rapporteurs appointments

## *5.1. Principles*

### 5.1.1. General principles for appointment of rapporteurs – centralised procedure

- All Members and alternates can act as rapporteur/co-rapporteur. (Note: Alternates of patient representatives and healthcare professionals cannot be rapporteurs at the PRAC).
- The rapporteur/co-rapporteur shall be supported by a team of assessors/experts (assessment team) during the various phases of the assessment of the application. The resources of the

rapporteur/co-rapporteur's assessment team shall be assessors/experts available not only from the rapporteur/co-rapporteur NCAs' level, but could be available from across the EEA. The use of multinational assessment teams, (with provisions in place at level of EMA for division of fees (for initial applications at current time) between participating NCAs) is strongly encouraged, as a means of increasing capacity, competence and collaboration in the EU regulatory system.

- The appointment of the rapporteur/co-rapporteur shall be made on the basis of objective criteria, which will ensure the provision of objective scientific opinions and will allow the use of the best and available expertise in the EEA in the relevant scientific area, over the lifecycle of the medicinal product.
- Members and alternates from the concerned committees are invited to indicate their interest in rapporteur/co-rapporteurships.
- The committee Chairperson in consultation with the Chairperson of other involved committees will decide on the final rapporteur/co-rapporteur and their assessment team appointment as applicable.
- The rapporteurs and co-rapporteurs are bound to the EMA Rules on the handling of declared interests.
- For any scientific evaluation in respect of an application submitted under the centralised procedure, the following shall be appointed:

| Procedure | CHMP rapporteur | CHMP co-rapporteur | PRAC rapporteur | PRAC co-rapporteur | CHMP Pharmaco-vigilance rapporteur |
|---|---|---|---|---|---|
| Full application | Delegation A | Delegation B | Delegation X[1] | Delegation A | - |
| Similar biological medicinal product | Delegation A | Delegation B | Delegation of reference product | - | - |
| Generics | Delegation A | None | Delegation of reference product[2] | - | Delegation of reference product[2] |
| Hybrids | Delegation A | On a case-by-case basis | Delegation of reference product[2] | - | Delegation of reference product[2] |

- For initial applications for ATMPs, the Rapporteur and Co-Rapporteur are appointed from the CAT, following the same appointment process. In such cases, two CHMP Coordinators are appointed from the same Delegation as the CAT Rapporteur and Co-Rapporteur.

### 5.1.2. Additional Principles for Generics/Hybrids

The following additional principles are considered for the appointment of rapporteurs/co-rapporteurs[3] and their assessment teams:

**Appointment of CHMP rapporteur/co-rapporteur**[3]

[1] For applications submitted pre-September 2012, until the re-appointment of the PRAC Rapporteur, the PRAC Rapporteur and Co-Rapporteur will come from the same delegation as the CHMP Rapporteur and Co-Rapporteur. See Annex 2.
[2] Depending on the regulatory route of authorisation of the reference medicinal product – see table in section 5.1.2.
[3] The appointment of a co-rapporteur for hybrids is handled on a case-by-case basis.

- The scope of these rapporteurships shall relate to the pre-authorisation phase and the introduction of quality changes in the post-authorisation maintenance.
- In order to ensure and facilitate consistency in the scientific evaluation/post authorisation maintenance of the medicinal products concerned, in the event that more than one application is received for a generic product with the same active substance, priority should be given to the appointment of the CHMP rapporteur in accordance to the following principles:
  - The same rapporteur for applications based on the same dossier.
  - A rapporteur for another generic with the same active substance.
  - A peer reviewer for another generic application with the same active substance.
- For several different generic applications with the same active substance a group of rapporteurs/peer reviewers shall be identified following the principles outlined above. Ideally this group shall consist of three to four CHMP members, depending on the number of applications received.
- In case information about the same bioequivalence study used in several generic applications becomes available after the appointment of different rapporteurs, the appointment of rapporteurs will be reconsidered. The first appointed rapporteur for the concerned generic products will receive the rapporteurship for all generic products with the same bioequivalence study.
- The EMA Secretariat shall handle and finalise all other post-authorisation activities (i.e. "administrative" harmonisation between the reference and the generic/hybrid medicinal product). These post-authorisation activities refer to the implementation of product information (SmPC/labelling/PL) changes of the generic/hybrid medicinal product following changes of the reference medicinal product. These changes might be following safety variation(s)/urgent safety restriction(s) of the reference medicinal product.
  This approach is by analogy to the Type IA variation approach in the centralised procedure.

**Appointment of CHMP pharmacovigilance rapporteur and PRAC rapporteur**

- For pharmacovigilance surveillance activities of generic/hybrid medicinal products, a CHMP pharmacovigilance rapporteur and a PRAC rapporteur shall be appointed.
- Where the reference medicinal product is a centrally authorised product, the PRAC rapporteur and the CHMP pharmacovigilance rapporteur shall be the same as those previously appointed for the reference medicinal product.
- Where the reference medicinal product is not centrally authorised, the appointment of the PRAC rapporteur and the CHMP pharmacovigilance rapporteur will depend on the regulatory route of authorisation of the reference medicinal product (see table below).

| Reference Medicinal product | PRAC or CHMP pharmacovigilance rapporteur |
|---|---|
| Centrally authorised medicinal product | Shall be the same as the previously appointed rapporteur for the reference medicinal product. |
| Product authorised through a Mutual Recognition/ Decentralised procedure (MRP/DCP): | Shall be a CHMP/PRAC Member representing the Reference Member State (RMS) where the reference medicinal product has been authorised.<br>In the case that there are several Reference Member States for the same concerned reference medicinal product, CHMP/PRAC Members represented by these delegations shall try to reach an agreement |

| Reference Medicinal product | PRAC or CHMP pharmacovigilance rapporteur |
|---|---|
| | between themselves on who will take the rapporteurship, respecting any prior discussion/agreement within the CMDh. |
| Product authorised through a National procedure: | Shall be a CHMP/PRAC member representing an EEA National Authority where the reference medicinal product has been authorised, respecting any prior discussion/agreement within the CMDh. |

- In order to enable/facilitate consistency in the pharmacovigilance monitoring/processing and follow-up of the medicinal product(s) concerned, in the event that more than one application is received for a generic product with the same active substance, the same PRAC rapporteur and CHMP pharmacovigilance rapporteur shall normally be appointed for the same active substance(s).

**Appointment of CHMP peer reviewer**:

- Where several generics of the same active substance are expected a CHMP peer reviewer shall be appointed for each generic/hybrid application in order to ensure consistency.
- The CHMP peer reviewer shall be one of the CHMP rapporteurs appointed for another generic with the same active substance. If no CHMP rapporteur appointed for another generic with the same active substance is interested to take the role of CHMP peer reviewer, the rapporteur for the reference medicinal product or a CHMP member who expressed interest shall be appointed in accordance with the principles outlined in section 5.1 of this paper.

### *5.2. Objective criteria*

The appointment of rapporteurs/co- rapporteurs and their assessment teams shall be made on the basis of objective criteria, which will ensure the provision of objective scientific opinions and will allow the use of the best and available expertise in the EEA in the relevant scientific area.

**The objective criteria outlined in this paper are identified as:**

- **Ability of rapporteur/co- rapporteur to fulfil their role**, which refers mainly to their ability to take responsibility for the scientific assessment /evaluation undertaken by the assessment team, coordination input etc.
- **Assessment team objective criteria** which refer to the scientific competence, regulatory experience, complementary cross-team scientific expertise and competence of the assessment team(s) as well as the availability of an adequate Quality Assurance System at the level of the EEA NCAs.
- **Individual objective criteria**[4] which refer to the academic expertise and the practical working experience and competence of the:
  - Individual assessor(s)/expert(s).
  - Rapporteur/co-rapporteur (when acting as assessor/expert in the scientific assessment of the application).

## 5.2.1. Assessment Team Objective Criteria

The following assessment team objective criteria shall be taken into consideration on the appointment of the rapporteur/co-rapporteur assessment team(s):

[4] The main criteria are the overall competence (scientific/regulatory) of the team to handle the scientific assessment and the Quality Assurance System of the NCA.

- **Scientific competence** of the team(s) in the handling of particular aspects[5] of the MAA, such as:
  - Methodological/statistical aspects.
  - Risk management/pharmacovigilance aspects.
  - Environmental risk toxicity.
- **Regulatory experience** such as:
  - Experience in the review of dossiers, preparation and provision of assessments reports for central and/or national applications in the relevant scientific area.
  - Ability to deliver assessment reports on time and in accordance with templates and timetables agreed and adopted by the committee, and/or specified for the particular procedure(s) as defined in the European Pharmaceutical Legislation.
  - Experience in peer review of Assessment Reports/Lists of Questions.
  - In case of non-prescription medicinal products: Experience with non-prescription medicinal products assessment; Experience with changes in legal status; Involvement at national level with same active substance(s) or rest of the therapeutic class as a non-prescription medicinal product coming for a central application; Experience in communication with patients.
- **Sufficient cross-team complementary expertise:**

  The need for additional input from (external/internal) assessors/experts during the assessment and/or in the post-authorisation phase should be transparent and their scientific/regulatory competence should be ensured, since they will be part of the assessment team (see also Section 5.1 of this Paper, Principles).
- **Quality Assurance System (QAS)**

  Availability of an adequate QAS ensuring an optimal quality of the scientific assessment and also regulatory consistency.

### 5.2.2. Individual Objective Criteria

- Individual objective criteria shall be taken into consideration for the appointment of rapporteur/co-rapporteur and their assessment team(s).
- Individual assessor(s)/expert(s) should have specific and in depth scientific expertise and competence. Direct working experience in the relevant scientific area and regulatory experience are preferable (see Annex 1 of this Paper).
- The competence of the individual assessor(s)/expert(s) would address, as appropriate, aspects of the quality, safety, efficacy and pharmacovigilance, as applied to the medicinal products. Sufficient cross team complementary experience should be taken into consideration (as described above in Section 5.2.1. of this Paper).

### 5.2.3. Proposed assessment teams with similar objective criteria

- In case of proposed assessment teams with similar objective criteria (scientific competence and availability), the following criterion will be used: even distribution based on a statistical overview, taking into account other procedures as well.

[5] In addition to the scientific competence aspects considered in the quality, safety and efficacy of a MAA.

- The experience with the appointment of rapporteur/co-rapporteur and their assessment teams shall be accumulated.

### *5.3. Methodology*

- The methodology for the appointment of rapporteurs and co-rapporteurs is detailed in SOP/H/3387 and SOP/H/3143. The timing of such appointment shall be as follows:

| Type of products | Initiation of appointment procedure | Appointment of rapporteur/co-rapporteur |
|---|---|---|
| Full Marketing Authorisations, similar biologicals | 7 months prior to the intended MAA submission date | 6 months prior to the intended MAA submission date |
| Generics/Hybrid | 3-7 months prior to the intended MAA submission date | 2-6 months prior to the intended MAA submission date |

# 6. Rapporteurship appointments for re-examinations

### *6.1. Additional Principles*

- Normally, a re-examination rapporteur and a co-rapporteur (CHMP/CAT and PRAC) shall be appointed.
- **A different CHMP/CAT rapporteur and, where necessary, a different CHMP co-rapporteur** from those appointed for the initial evaluation shall be appointed in order to assess the grounds for the re-examination of the CHMP opinion. These rapporteurs will coordinate the evaluation for the duration of the re-examination procedure only.
- For procedures where the co-rapporteur was not involved in the evaluation, no co-rapporteur for the re-examination shall be appointed.
- Regarding **centrally authorised products**, the appointed **PRAC rapporteur** will normally also act as rapporteur for the re-examination, unless the grounds for re-examination specifically concern issues of risk management. In such cases, the PRAC rapporteur will be from the same delegation as the CHMP re-examination rapporteur.
- Regarding re-examination requests for **referrals assessed by the PRAC under Article 31 of Directive 2001/83/EC**, a **different** PRAC Rapporteur, and where necessary, a different co-rapporteur from those appointed for the initial evaluation shall be appointed in order to assess the grounds for the re-examination of the PRAC recommendation
- The principles outlined in section 5 of this Paper shall apply.
- The objective criteria as discussed in the relevant sections of this Paper shall apply.

### *6.2. Specific Methodology*

- The rapporteur, co-rapporteur (if applicable) appointment process will be initiated as soon as the EMA/CHMP/PRAC receive written notice that the applicant/MAH wishes to request a re-examination of the CHMP opinion/PRAC recommendation.

- Strict timeframes apply as there is no clock stop in the re-examination procedure and the maximum timeframe is 60 days (please refer to the CHMP Guideline on re-examination CHMP/50745/2005).

# 7. Rapporteurship appointments for referral procedures

## *7.1. Additional Principles*

- Due to the particularities of the referral procedures (such as non-predictability of a referral notification), with consequences on the workload and availability of CHMP and PRAC members and alternates, the following additional principles shall be considered for the appointment of CHMP/PRAC rapporteur/co-Rapporteur:

### 7.1.1. Referrals assessed by CHMP

The principles outlined in Sections 5.1 and 5.2 of this paper shall apply, in addition to the following ones:

- Normally, for the scientific evaluation in respect of a referral procedure a CHMP rapporteur and a CHMP co-rapporteur shall be appointed (as appropriate).
- In the case of class referrals involving several active substances, a lead rapporteur and more than one co-Rapporteur could be appointed. The role of the lead rapporteur would primarily be to prepare an overall Assessment Report, considering all active substances, and taking into account the assessment reports from each co-rapporteur.
- The following shall be considered for the appointment of CHMP rapporteur/co-rapporteur as per the particular referral procedure:

| Article | Rapporteur | Co-Rapporteur |
|---|---|---|
| Article 13 of Commission Regulation (EC) No 1234/2008[6] | Open to all CHMP members | Open to all CHMP members |
| Article 20 of Regulation (EC) No 726/2004 | CHMP rapporteur already identified for the CAP(s)[7] | CHMP co-rapporteur already identified for the CAP(s)[7] |
| Article 29 of Directive 2001/83/EC | CHMP member from the Reference Member State | CHMP member from a concerned (divergent) Member State |
| Article 29 of the Paediatric Regulation No 1901/2006 | Open to all CHMP members | Open to all CHMP members |
| Article 30 of Directive 2001/83/EC[8] | CHMP member from the triggering Member State or open to all members if EC triggers the referral | Open to all CHMP members |

[6] In this referral the National Competent Authorities concerned by the medicinal product application are of the opinion that the variation cannot be accepted and the MAH may trigger a referral.
[7] If at least one CAP is involved in the referral, the CHMP rapporteur already identified for the CAP will be appointed (at the discretion of the CHMP Chairperson). If more than one CAP is involved in the same referral, the CHMP referral (co-) rapporteur shall be appointed from amongst the CHMP (co-) rapporteurs for the CAPs involved in the referral.
[8] In this referral, divergent decisions have been taken by the Member States related to the particular medicinal product.

| Article | Rapporteur | Co-Rapporteur |
|---|---|---|
| | | |
| Article 31 of Directive 2001/83/EC[9] | CHMP rapporteur already identified for the CAP(s)[7] or if no CAP(s) involved, open to all CHMP members | CHMP co-rapporteur already identified for the CAP(s)[7] or Open to all CHMP members |
| Article 5(3) of Regulation (EC) No 726/2004 | CHMP rapporteur already identified for the CAP(s)[7] or if no CAP(s) involved, open to all CHMP members | CHMP co-rapporteur already identified for the CAP(s)[7] or open to all CHMP members |

- The CHMP Chairperson will decide on the final appointment of rapporteur/co-rapporteur based on members volunteering and will propose it to the committee.
- If no CHMP member volunteers (as applicable) in the rapporteur/co-rapporteur appointment procedure, the CHMP Chairperson will propose the CHMP rapporteur/CHMP co-rapporteur.

### 7.1.2. Safety Referrals assessed by PRAC: Urgent Union procedures (Article 107i), Article 31 Pharmacovigilance and Article 20 Pharmacovigilance[10]

The principles outlined in Sections 5.1 and 5.2 of this paper shall apply, in addition to the following ones:

- Normally, for the scientific evaluation in respect of such referral procedures, a PRAC rapporteur and a PRAC co-rapporteur shall be appointed.
- In the case of class referrals involving several active substances, a lead rapporteur and more than one co-Rapporteur could be appointed. The role of the lead rapporteur would primarily be to prepare an overall Assessment Report, considering all active substances, and taking into account the assessment reports from each co-rapporteur.
- The following shall be considered for the appointment of PRAC rapporteur/co-rapporteur as per the particular referral procedure:

| Article | Rapporteur | Co-rapporteur |
|---|---|---|
| Article 20 of Regulation (EC) No 726/2004 | Priority given to the PRAC rapporteur already identified for the CAP(s)[11] | Priority given to the PRAC co-rapporteur already identified for the CAP(s)[11] |
| Article 31 of Directive 2001/83/EC | Open to all PRAC members[12] | Open to all PRAC members |

[9] In this referral, interests of the Union are involved.
[10] The PRAC recommendations for Article 31 and Article 107i referral procedures including at least one marketing authorisation granted in accordance with the centralised procedures are presented for adoption to the CHMP by the CHMP Member from the delegation of the PRAC rapporteur. The PRAC recommendations for Article 31 and Article 107i referrals procedures not including at least one marketing authorisation granted in accordance with the centralised procedures are presented to the CMDh by the CMDh member from the delegation of the PRAC rapporteur for adoption.
[11] If more than one CAP is involved, the PRAC referral (co-) rapporteur shall be appointed from amongst the PRAC (co-) rapporteurs for the CAPs involved in the referral. Note: In case the referral procedure is not product specific, the PRAC Chairman may advise to open Rapporteurship to all PRAC members
[12] The rapporteurship is not open to the Member State who triggered the referral. The triggering Member State may bid for Co-Rapporteurship but will not be appointed by default.

| Article | Rapporteur | Co-rapporteur |
|---|---|---|
| Articles 107i of Directive 2001/83/EC | Open to all PRAC members[12] | Open to all PRAC members |

- The PRAC Chairperson will decide on the final appointment of PRAC rapporteur/co-rapporteur.
- If no PRAC member volunteers in the rapporteur/co-rapporteur appointment procedure, the PRAC Chairperson will propose the PRAC rapporteur/PRAC co-rapporteur.

### *7.2. Specific Methodology*

- Normally, the CHMP or PRAC rapporteur/co-rapporteur appointment process (as applicable) will be initiated as soon as the EMA/CHMP/PRAC receive the referral notification.
- In case the referral notification is received during a CHMP/PRAC meeting and depending on the urgency of the matter (e.g. notification of safety issue(s)), the CHMP or PRAC rapporteur/co-rapporteur appointment process may take place during such meetings (as applicable).

### *7.3. Appointment of rapporteurs for re-examinations of referral procedures*

- For referrals procedures, re-examination requests are foreseen for referrals under Articles 29, 30, 31 of Directive 2001/83/EC and for Article 13 of Commission Regulation No 1234/2008 only.
- The procedure for the re-examination of a referral is the same as available earlier in sections 6.1 and 6.2 of this document.

## 8. Rapporteurship appointments for signals

### *8.1. Additional principles*

| Type of product | Rapporteur |
|---|---|
| Centralised products | PRAC rapporteur as identified for the centralised product |
| Nationally authorised products included in List | PRAC member from Member State identified in the List of active substances subject to worksharing for signal management. |
| Products which are not on the list (i.e. no lead delegation) – i.e. Nationally authorised products or signals referring to a therapeutic class (either mix of Centralised and Nationally authorised products or Nationally authorised products only) | Priority given to the PRAC Member from Member State who confirmed the signal[13].<br>For signals referring to a therapeutic class, the Rapporteur can also be one of the identified PRAC rapporteurs for any centralised product or lead Member States identified for substances part of the List of active substances subject to worksharing for signal management. |

[13] Subject to ability/availability of Member State to take on this role. In case of non-availability, open to all PRAC members.

For products, where no lead delegation has been identified (i.e. not included in the List of active substances subject to worksharing for signal management), the appointment of Rapporteur will be confirmed at the first meeting at which the signal is discussed.

# 9. Rapporteurship appointments for PSURs/PSUSAs

## *9.1. Additional principles for CAP(s), CAP(s)/NAP(s)*

| Type of product | Rapporteur |
|---|---|
| For active substances as identified in the list of Union Reference Dates and frequency (EURD) list with Centrally Authorised products only | PRAC rapporteur as identified for the centralised product[14] |
| For active substances as identified in the list of Union Reference Dates and frequency (EURD) list with Centrally and Nationally Authorised products involved | Priority given to the rapporteur of the first approved centralised product[15] |

For active substances as identified in the list of Union Reference Dates and frequency (EURD) list with Centrally and Nationally Authorised products involved, the Rapporteur is appointed 6 – 7 months in advance of planned submission.

Note: With respect to Periodic Safety Assessment Report (PSUR) single assessment procedures (PSUSAs) involving nationally authorised products only, the CMDh is responsible for the appointment of a Lead Member State.

# 10. Rapporteurship appointments for imposed Post-Authorisation Safety Study (PASS) protocols and results

## *10.1. Additional principles*

| Type of product | Rapporteur |
|---|---|
| PASS protocol and results for a Centrally Authorised Product | PRAC rapporteur as identified for the centralised product |
| PASS protocol (and results) imposed as a result of a safety referral and conducted in more than 1 Member State | Priority will be given to the PRAC rapporteur for the referral |
| PASS protocol (and results) imposed by Member States and conducted in more than 1 Member State | Priority will be given to Member State who imposed the obligation on the MAH |

[14] Where there is more than one CAP, priority is given to the rapporteur of the first approved centralised product
[15] In case other members would express an interest in taking on the Rapporteurship, the PRAC Chairperson will decide on the final appointment of rapporteur

For Nationally Authorised products, including those authorised via MRP/DCP, a PRAC Rapporteur will be appointed upon receipt of a PASS protocol submission. The name of the appointed PRAC Rapporteur will be communicated to the Marketing Authorisation Holder during the EMA check (period defined between the submission and the start of the procedure).

# 11. Changes affecting the appointment of rapporteur/co-rapporteur

The following issues may be encountered and affect the appointment of rapporteur/co-rapporteur:

- **Applicant informs the EMA on a revised intended MAA submission date:**

  Applicant informs the appointed rapporteur/co-rapporteur and committee Secretariat in writing.

  If appointed rapporteur and/or co-rapporteur and their assessment teams are no longer available, a new appointment procedure shall take place. Otherwise, the availability of appointed rapporteur/co-rapporteur and their assessment teams will remain as is.

- **A previously withdrawn MAA is re-submitted:**

  A new appointment procedure of rapporteur/co-rapporteur shall take place.
  Note: There is no automatic link to the previously appointed rapporteur/co-rapporteur and their assessment teams for such MAA.

- **Member State appointed member informs the Committee, at any time, that she/he is no longer as rapporteur/co-rapporteur available for the assessment:**

  Normally, the rapporteurship will be taken over by the successor committee Member or by his/her alternate to work with the previously identified assessment team.
  If this is not feasible, then a new appointment procedure of rapporteur/co-rapporteur and her/his assessment team shall take place.

- **Co-opted Member (CHMP) informs the committee, at any time, that she/he is no longer available as rapporteur/co-rapporteur for the assessment:**

  Co-opted Member affiliated to an EEA NCA:

  The EEA NCA to identify a Member/alternate to take over the responsibility for (co) rapporteurship and to work with the previously identified assessment team. The committee shall confirm this appointment.

  Co-opted Member not affiliated to an EEA NCA.

  The appointment procedure of rapporteur/co-rapporteur and her/his assessment teams shall take place.

- **Independent scientific expert (PRAC) informs the committee, at any time, that she/he is no longer available as rapporteur/co-rapporteur for the assessment:**

  The appointment procedure of rapporteur/co-rapporteur and her/his assessment teams to be considered on a case-by-case basis.

# 12. References

- Regulation (EC) No 726/2004 of the European Parliament and of the Council, of 31 March 2004
- Directive 2001/83/EC, as amended and its Annex I, of 6 November 2001
- Notice To Applicants, Volume 2A
- CHMP Rules of Procedure (EMEA/45110/2007)
- Procedural Advice to CHMP Members (EMEA/361945/2007)
- CAT Rules of Procedure (EMEA/CAT/454446/2008)
- PRAC Rules of Procedure (EMA/PRAC/488608/2012)
- Procedural advice on evaluation of Advanced Therapy Medicinal Products (ATMPs) (EMEA/630043/2008)
- EMA Pre-submission Guidance for users of the centralised procedure
- EMA Post authorisation Guidance
- Evaluation of conflicts of interests of experts for involvement in Agency activities (SOP/EMA/0040)
- Arrangements for handling of conflicts of interests for EMA scientific meetings (SOP/EMA/0126)
- EMA policy on the handling of conflict of Interests for EMA scientific committees Members and Experts (Policy/0044)
- The EMA code of conduct
- Guideline on re-examination (CHMP/50745/2005)
- Guideline on Similar Biological Medicinal Products (CHMP/437/04)
- Peer Review/Quality assurance of the Day 120 CHMP List of Questions and assessment reports (SOP/H/3015)
- Operation of the business pipeline activity for medicines for human use (SOP/H/3387)
- CHMP rapporteur/co-rapporteur/peer reviewer appointment in the centralised procedure (SOP/H/3143)
- Good pharmacovigilance practices
- 3174 WIN - Rapporteur Co-Rapporteur - Forthcoming applications for information to HMA-H

**Abbreviations**

- ATMPs Advanced Therapy Medicinal Products (ATMPs)
- CAP(s) Centrally Authorised Product(s)
- CAT Committee for Advanced Therapies
- CHMP Committee for Medicinal Products for Human use
- PRAC Pharmacovigilance Risk Assessment Committee
- CMDh Co-ordination Group for Mutual Recognition and Decentralised Procedures - Human
- DCP Decentralised procedure

- EEA European Economic Area
- EU European Union
- MAA Marketing Authorisation Application
- MAH Marketing Authorisation Holder
- MRP Mutual Recognition Procedure
- NAP(s) Nationally Authorised Product(s)
- NCA National Competent Authority
- PhV PharmacoVigilance
- PSURs Periodic Safety Update Report(s)
- PSUSAs Periodic Safety Update Report Single Assessment(s)
- PASSs Post-Authorisation Safety Studies
- QAS Quality Assurance System
- RMS Reference Member State
- SAGs Scientific Advisory Groups

## Annex 1

## Individual Objective Criteria to be taken into consideration for the appointment of the Rapporteur/Co-Rapporteur and their assessment teams.

### Individual Objective Criteria

The following Individual Objective Criteria should be considered for the appointment of the assessor(s)/expert(s):

- **Academic expertise** in the relevant scientific area, such as:

  Internationally recognised academic qualification(s) /accreditation(s) (e.g. Degrees, Diplomas, Post Graduate Qualifications (e.g. PhD), Professional Affiliations etc.)

  Delivering scientific expert views/opinions to National/European/International scientific bodies

- **Direct working experience** in the relevant scientific area, such as:

  Clinical Co-ordinator/Investigator in clinical trials

  Clinical expertise (e.g. specialisation) in the relevant area

  Pre-clinical research and expertise (e.g. in toxicology, pharmacology)

  Scientific research (e.g. in epidemiological studies, animal studies etc.)

  Research in the relevant "quality" areas, relating to the research and development of medicinal products (e.g. molecular biology, gene technology etc.)

  Formulation, manufacture and control of medicinal products

  Inspection (GXP inspections)

  Pharmacovigilance and Risk Management

  Targeted Publications in recognised and peer-reviewed scientific journals

  Peer Reviewing activities for scientific journals

  Advisory experience in committees'/scientific bodies' activities (e.g. experience in providing scientific advice for central and/or national MAs, involvement in WHO, EDQM, FDA activities etc.)

  Previous involvement in EU Commission activities, such as receipt of grants within the Framework Programs leading for example to publication in well recognised scientific journals

  Regulatory experience such as writing Assessment Reports, participating in Scientific Advice etc.

  Medical Device

  Involvement in changing the legal status of a medicine from prescription to non-prescription

  Regulatory experience with assessment of non-prescription medicinal product; experience in communication with patients

## Annex 2

## Appointment of PRAC Rapporteur: Centralised applications

The PRAC rapporteur and co-rapporteur will be appointed at the same time as the CHMP rapporteur and co-rapporteur/ CHMP peer-reviewer(s), if possible.

The following principles apply:

For Initial marketing applications

| | **CHMP** | **PRAC** |
|---|---|---|
| **Rapporteur** | **Delegation A** | **Delegation X** |
| **Co-rapporteur** | **Delegation B** | **Delegation A** |

For re-examination procedures

| | **CHMP** | **PRAC** |
|---|---|---|
| **Rapporteur** | **Delegation C** | **Delegation X**[16] |
| **Co-rapporteur** | **Delegation D** | **Delegation A**[16] |

[16] Same as per the initial marketing application