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"Quality Assurance in the CHMP"

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Quality Assurance in the CHMP

Peer review procedure

- Background: CHMP Audit A03015 and OFI A03015-02
- Quality Assurance of (Co)-Rapporteur assessment reports and related documents (List of questions)
- Initial phase: 15th April 2005
- EMEA SOP/H/3015
- The different scopes of CHMP members review and EMEA Staff comments are described in various forms:
  - " Instructions and Template for comments and peer review of the AR from (Co-) Rapporteurs" (Annex 1)
  - "Instructions and template for EMEA comments on the ARs from (Co-) Rapporteurs" (Annex 2)

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➢ Definition Peer review

- Peer review is a scholarly process used in the publication of manuscripts and in the awarding of funding for research
- Publisher's and funding agencies use peer review to select and to screen submissions
- The process also forces authors to meet the standards of their discipline and thus achieve scientific objectivity

(Source: Wikipedea)

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➢ Peer review procedure

- The EU MA procedure should be based on a high quality initial assessment supported by an adequate system of PR
- The need and scope of the PR will be decided on by CHMP on a case by case basis
- Members of the CHMP should be encouraged to participate as much as possible in such PR process.
- The PR concept should ensure a quality control on the initial assessment, without duplication of the assessment already conducted.

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Peer review procedure

- The PR should relate to the content and the format and should provide additional and complementary critical expertise to the initial assessment.
- The PR should be carried out in a
  - transparent
  - and a timely manner
- A revision of the peer review system will be initiated:
  - 3rd Q 2006

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SOP:

- **Peer review/QA of the Day 120 CHMP LoQs and ARs**
  - Describes the objectives and timing of comments in the period between the releases of the R/cR initial AR and the adoption of the LoQ
  - Describes the peer review as part of the QA system at CHMP level
  - Reviews the purpose of improving the Q of the day 120 LoQ by CHMP members assigned as peer reviewers

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- ***Instructions and template for EMEA comments on the AR from R/cR (1)***
- **Comments should be made in relation to clarity and consistency of the "overview and LoQ"**
  - Deletion of redundancies (Quality, Non clinical, Clinical)
  - Improvements of the questions regarding clarity and format
  - Attention to questions raised on similar products authorised via centralised procedure
  - Attention to relevant CHMP guidelines/ scientific advice
  - Improvement in the product information

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- ***Instructions and template for comments and peer review of the initial assessment reports from R/cR***
- **Peer reviewer (1)**
  - Contribution to the quality assurance of the LoQ intended for the applicant
  - Whole or selected parts of the Q/E/S assessment as decided by CHMP
  - A template should be used for the peer review

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- ***Instructions and template for comments and peer review of the initial assessment reports from R/cR***
- **Peer reviewer (2)**
  - **The extent to which the scientific argumentation in the R/cR Assessment reports supports the proposed questions in the LoQ**
  - **The consistency between issues raised in the day 120 LoQ and the CHMP guidelines/ Scientific advice and issues raised in the assessment of products within the same class/indication**

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- ***Instructions and template for comments and peer review of the initial assessment reports from R/cR***
- **Peer reviewer (3)**
  - **Proposals to modify and improve the LoQ together with parts of the AR, conclusions/benefit risk assessment, overview and SmPC could be made by PR**
  - **However, the R/cR remain responsible for the content of the different parts of the AR's and the proposed Overview and LoQ and will consider what changes to be considered for inclusion in the documents**

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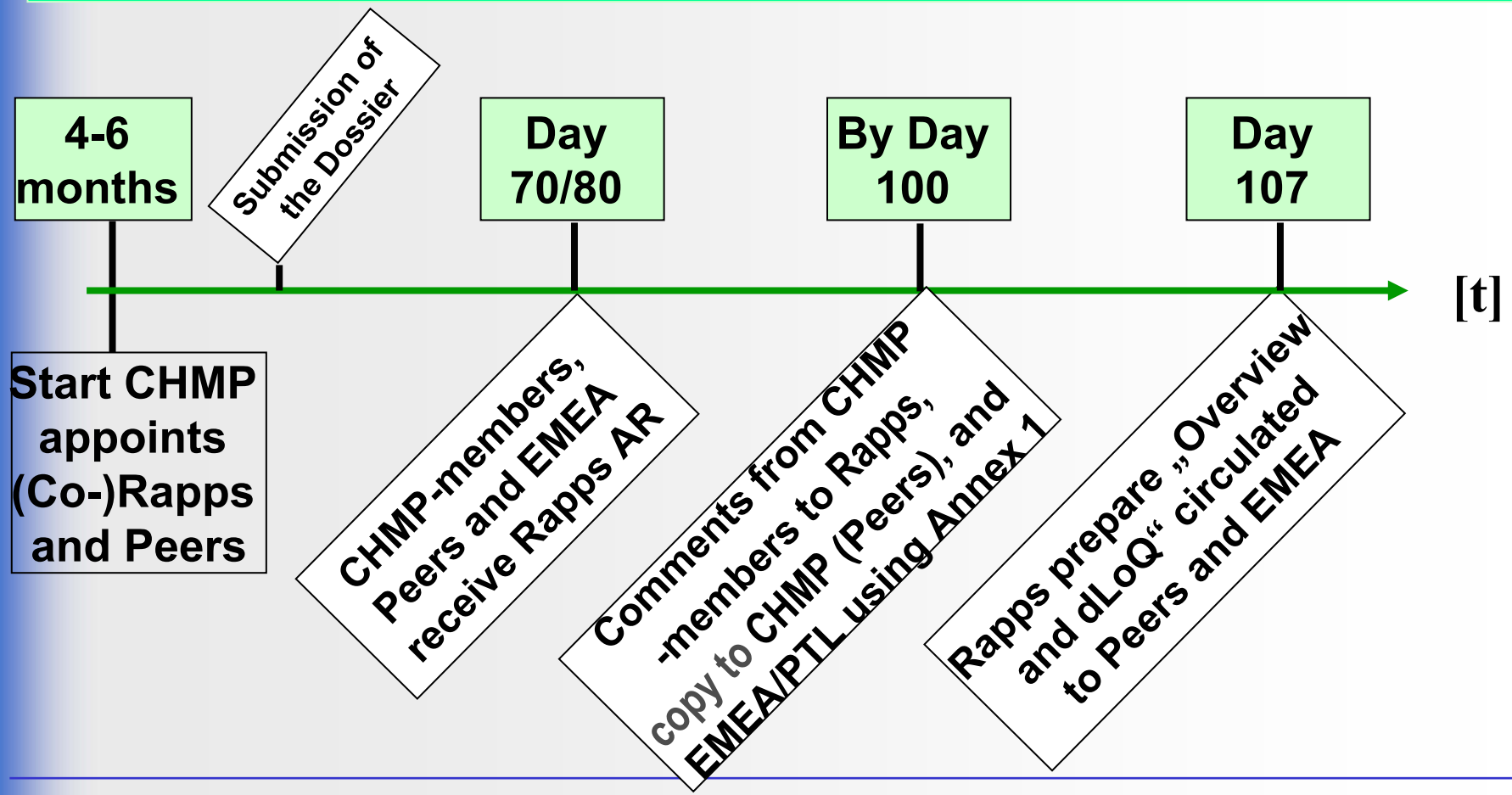
Timetable for Peer Review QA of D120 CHMP LoQ and AR



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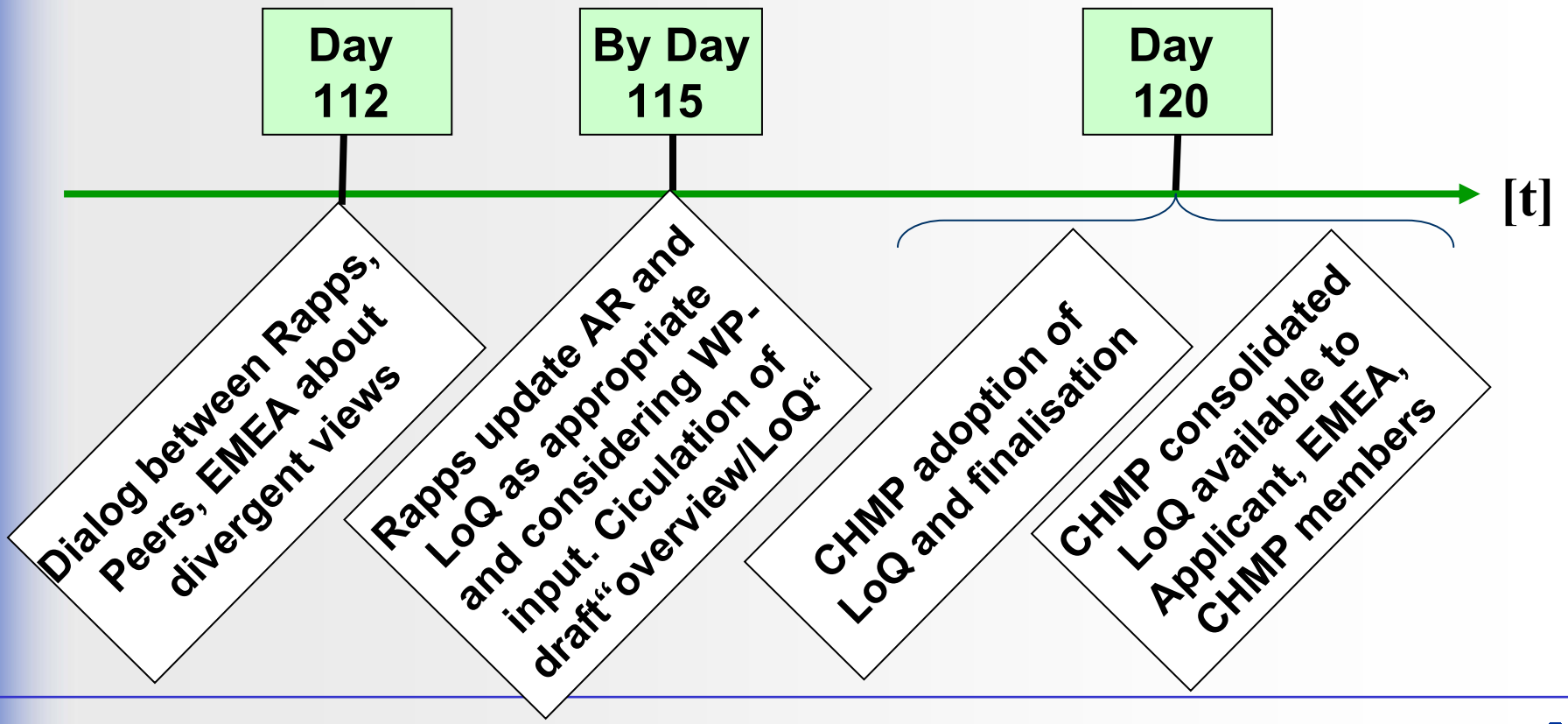
Timetable for Peer Review QA of D120 CHMP LoQ and AR



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- Example

CHMP PLENARY MEETING 23 - 26 MAY 2005
RAPPORTEURSHIP / PEER REVIEW
DRAFT OUTCOME

Rapporteurship

Requests received from: SE, ES, DE, IT, UK, NL, FR, DK
No requests received from: AT, BE, CZ, CY, EE, FI, GR, HU, IE, LV, LU, LT, MT, PL, PT, SK, SI, IC, NO

Peer Review

Requests received from: SE, DE, NL, UK, HU, CZ,
No requests received from: AT, BE, CY, DK, EE, FI, GR, IE, LV, MT, PL, SK, SI, IC, NO, PT, ES, IT, LT, LU, FR

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Name of the Product	Company's Rapporteur-ship priorities	Priority for Rapporteur-ship	Priority for Co-Rapporteur-ship	Priority for Peer Review
Invented name (INN), company, EMEA PTL, PTM. Invented name is indicated for the treatment of patients. Pharmaceutical form: Orphan Medicinal Product designation. Intended date of submission by: 3Q 2005. *Orphan*.	Dr Abadie Dr Salmonson	1. Priority [SE, FR] 2. Priority [UK] 3. Priority [DE, NL]	1. Priority [SE] 2. Priority [] 3. Priority [DE, NL]	1. Priority [SE, DE] 2. Priority [] 3. Priority []
PROPOSAL	**Rapporteur: Dr Abadie** **Co-Rapporteur: Dr Salmonson** **Peer Reviewer: Dr Enzmann**			

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- Assignment of Rapporteurship (1)
- Current Rules of R/cR Appointment: Legal Framework, Methodology on Rapp./ Co-Rapp. Appointment
- Future practice: legal frame work, legal scope of the future practice, key issues of proposed practice

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➢ Assignment of Rapporteurship (2)

➢ Current practice

- **Legislative framework: Council Regulation (EEC) No 2309/93**
- Article 53(1)

  *"…the Committee shall appoint one of its members to act as **rapporteur** for the co-ordination of the evaluation, taking into consideration any **proposal from the applicant** for the choice of rapporteur. The committee may appoint a second member to act as **co-rapporteur**. The Committee shall ensure that **all its members** undertake the role of rapporteur or co-rapporteur."*

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Assignment of Rapporteurship (3)

- Council Regulation (EEC) No 2309/93, Article 52(1)
  *"The CHMP shall each consist of two members nominated by each Member State… They shall be chosen by reason of their **role and experience in the evaluation** of medicinal products…as appropriate and shall represent their competent authorities".*

- Council Regulation (EEC) No 2309/93, Article 52(3)
  *"The members of the Committees and the experts responsible for **evaluating** medicinal products shall rely on the **scientific assessment and resources** available to the national marketing authorisation bodies*

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- **Assignment of Rapporteurship (4)**

- **Current rules of R/cR Appointment**

1. Each CHMP meeting
2. ~ 6 months prior submission
3. Applicant may propose 3-4 names of CHMP Members
4. Reconciliation between applicant's preferences and CHMP Member's requests
5. One Member is appointed as R and one as cR
6. Even distribution→statistical overview
7. R/cRs appointments accumulated in the 3 year CHMP "term"

- **CHMP Chairman's discretion is practiced in appointment process**

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➢ Assignment of Rapporteurship (5)

➢ Future practice

- **Legislative framework:** Regulation (EC) No 726/2004

- Article 62 (1):
  *"… the Committee for Medicinal Products for Human Use,…, it shall appoint one of its members to act as **rapporteur** for the coordination of the evaluation. The Committee concerned may appoint a second member to act as **co-rapporteur**."*

- **NEW!**➔ New Legislation is silent considering any proposals from the applicants

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- **Assignment of Rapporteurship (6)**

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

- Article 57(1):
  "***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…".***

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- **Assignment of Rapporteurship (7)**

- **NEW!** CHMP Rules of Procedure, Article 6:
  "… The appointment of the rapporteur shall be made on the basis of ***objective criteria****, which will allow* ***the use of the best available expertise in the EU*** *on the relevant scientific area."*

- Article 61(5):
  "In addition to their task of providing ***objective scientific opinions*** *…, 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."*

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- **Assignment of Rapporteurship (8)**

- Article 61(6):
  *"Members of the committees and experts responsible for evaluating medicinal products shall rely on the **scientific evaluation and resources** available to national marketing authorization bodies."*

- **NEW!** CHMP Rules of Procedure, Article 6.4:
  *"The rapporteur, and when appropriate, co-rapporteur chooses.... his/her/their assessment team. He/she/they notify his/her/their choice to the EMEA **prior to the start of the procedure**".*

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- **Assignment of Rapporteurship (9)**

- Article 62(3):
  "The provision of services by rapporteurs or experts shall be governed by a written contract…. The person concerned, or his employer, shall be remunerated..."

- **NEW!** Article 62(4):
  *"The performance of scientific services for which there are several potential providers may result in a call for an **expression of interest**, if the scientific and technical context allows, and if it is compatible with the tasks of the Agency, in particular to ensure a high level of public health protection."*

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➢ Assignment of Rapporteurship (10)

SCOPE OF FUTURE PRACTICE

The key issues to be considered on R/cR appointment:

- Applicant's proposals→**not** to be considered
- Appointment on the basis of **objective criteria**→
  use of the best available expertise **in the EEA**

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Develop principles and objective criteria

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➢ **Optimum performance of scientific services** and the use of **best available expertise**

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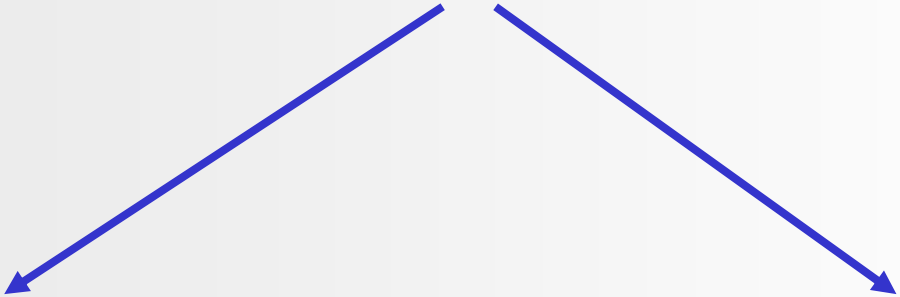
2-phase approach



First phase

Preparatory step

Second phase

Appointment of R/cR
+Assessment Teams

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- **First phase:**
  - **Early preparatory** step
  - **Indicator** of subsequent appointment (R/cR +Assessment Teams)
  - **Pre-awareness** step
  - **Not** necessarily **prejudge** the appointment of the Second phase

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- **First phase:**
  - **Indicate scientific competence on** specific therapeutic/technological area(s)
  - **Stimulate** proactive and longer term scientific **resource planning**
  - **Identify** potential **difficulties** and **facilitate resolutions**
  - Build an **overall profile** of capacity and system in place for scientific assessment resources, if desired by the NCAs

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- **First phase:**
- **Twice a year**
  - In July of each year, ➔ estimate of applications expected in the coming 18 months
  - In January of next year➔, revised estimate of applications expected in the coming 12 months

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- **Second phase:**
  - Actual appointment process
  - When➔7 months prior to submission date
  - CHMP Members express nominations for R/cR and their assessment teams➔
  - CHMP appoints R + assessment team and cR + assessment team

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- **Second phase:**

Appointment on the basis of **objective criteria**→
use of the best available expertise **in the EEA**

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Develop principles and objective criteria

Principles: New legislation

Objective criteria: Role of R/cR, Assessment Team and Individual

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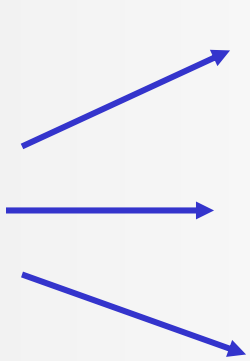
- **Second phase:**

Objective criteria:



Role of R/cR

Assessment Team

Individual

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➢ Second phase:

Principles→ **Role of R/cR** mainly to:

- **Coordinate input**
- **Take responsibility for scientific assessment**
- **Involve additional expertise (PhV, PMS/RMP)**
- **Provide objective scientific opinions**
- **Identify post authorisation measures**
- **Spokesman with applicant(s)**
- **Good interaction with EMEA/PTL/PTM**
- **Establish contact with Patient Organisations /HC Professionals**

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- **Second phase:**
- Assessment Team Objective Criteria:
  - **Scientific competence of the Team**
  - **Regulatory experience of the Team**
  - **Complementary cross-team scientific expertise and competence of the Team**
  - **Availability of an adequate Quality Assurance System at the level of all EEA NCAs**

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- **Second phase:**
- Individual Objective Criteria:
  - **Academic expertise**
  - **Direct working experience and competence**

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  - **Assessor/expert and R/cR (if acting as assessor/expert)**

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➢ Second phase:

- If similar objective criteria (scientific/regulatory competence + availability)

  ➔ even distribution (statistical overview)

- Choice between R-cR:

  Ability to manage post authorisation issues

  (PMS, PhV plan)

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Development of draft Reflection Paper