1 March 2013
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Management Board meeting of 21 March 2013

Renewal of the mandate for the Joint Expert Group on 3Rs

Issues for consideration

At its October 2010 meeting the Management Board endorsed the formation of the Joint CVMP/CHMP ad hoc expert group on the application of the 3Rs (replacement, reduction, refinement) in regulatory testing of medicinal products, with for initial period of 2 years.

Since that time the JEG 3Rs has provided a valuable forum for the development of strategies aimed at ensuring best practice with regards to the use of experimental animals within the field of regulatory testing of medicines while also demonstrating the Agency's engagement in this area. The Board's endorsement for the continued activity of the group for a further 2 years is now sought. In addition the board is asked to endorse the inclusion of an HMPC representative in the group.

The activities of the group over the next two years will focus particularly on the following three areas:

- compliance of existing animal testing guidance with 3Rs principles and the development of guidance relating to the acceptance of 3Rs testing paradigms,
- 3Rs issues related to batch release testing, and
- supporting implementation of Directive 2010/63/EU

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EMA/CHMP/CVMP/JEG-3Rs/442724/2012

Terms of reference, objectives and rules of procedure for the joint CVMP/CHMP ad hoc expert group on the application of the 3Rs (replacement, reduction and refinement) in regulatory testing of medicinal products (JEG 3Rs)

1. General considerations

The CVMP and CHMP Rules of Procedures state, in article 18, that "When necessary, the Committee, its working parties and scientific advisory groups may avail themselves of the services of experts in 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 expert's list".

In line with the above quoted article, an ad hoc expert group can be established in order to provide advice on scientific/technical matters related to the regulatory testing of medicinal products for human and veterinary use under the responsibility of CHMP and CVMP.

At its October 2010 meeting the EMA Management Board endorsed the formation of an ad hoc expert group on the application of 3Rs in the development of medicinal products, for an initial term of 2 years. At its March 2013 meeting the EMA Management Board endorsed the group's continued activity for a further 2 years. As the issues relating to the 3Rs concern both veterinary and human medicines it is appropriate for any group focussing on this area to be a joint CVMP/CHMP group.

It is recognised that much work is already being done in the 3Rs area by other European Commission bodies (particularly EURL ECVAM) and European organisations such as EDQM and it is therefore important to ensure that the Agency group should complement and not duplicate the work.

2. Terms of reference and objectives

The JEG 3Rs was established to improve and foster the application of 3Rs in the regulatory testing of medicinal products throughout their lifecycle. The group provides advice and recommendations to the Committees on all matters relating to the use of animals in regulatory testing of medicinal products including, but not limited to, the tasks defined below:

- Identification of opportunities for implementation of 3Rs in regulatory testing
- Coordinating, facilitating and prioritising EMA activities within the 3Rs arena
- Supporting implementation of Directive 2010/63/EU

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- Establishing strong ties with EDQM and EURL ECVAM
- Contributing to development of guidelines in which 3Rs issues are applicable in collaboration with relevant Working Parties
- Providing information and advice on 3Rs to stakeholders
- Considering how progress on 3Rs issues can most usefully be used to influence development of regulatory guidance at an international level through ICH, VICH etc

In 2013 and 2014 the JEG 3Rs will particularly focus on the following three areas: (1) compliance of existing animal testing guidance with 3Rs principles and the development of guidance relating to the acceptance of 3Rs testing paradigms, (2) 3Rs issues related to batch release testing, and (3) supporting implementation of Directive 2010/63/EU. More detail on the specific projects in which the JEG 3Rs is actively involved is provided in the work plan.

3. Composition and rules of participation

- The core of the JEG 3Rs consists of experts nominated by CVMP, CHMP, relevant Working Parties and HMPC, and will be complemented, as necessary, by specified experts. Relevant Working Parties are considered to be QWP, SWP, BWP, VWP, SWP-V, EWP-V, IWP-V. All JEG 3Rs members are included in the EMA European Experts list.
- In order to ensure that the objectives of the ad hoc expert group can be accomplished, all relevant disciplines (i.e. quality, safety and, in the case of veterinary medicinal products, efficacy) are represented, for both pharmaceutical and biological/immunological products.
- As membership of the group is made up of one, or at most two, members from the Committees and Working Parties named above, the continued participation of up to 15-20 members is expected.
- EDQM and EURL ECVAM are invited to send a representative each to the meetings to act as observers.
- Representatives of DG Environment may also be invited to attend meetings as observers in order to facilitate discussions relating to Directive 2010/63/EU.
- Membership of the group implies a commitment to participate actively in the group's work and to attend meetings of the group regularly.
- A member may nominate a replacement to participate in those exceptional cases where he or she is unable to attend a meeting.
- Members who want to bring additional experts should notify the Agency Secretariat in advance of the meeting, and receive the agreement of the chairperson for the participation of the additional experts.
- Meeting documentation will be distributed to an agreed list of recipients drawn up by the Agency with the agreement of the chairperson.
- Observers from non-EEA countries and accession countries may participate with the agreement of the chairperson and the Agency. Specific confidentiality rules will apply to observers.

4. Meeting frequency

The expert group will meet two times per year for one day meetings, where possible immediately before or after CVMP, CHMP, Working Party or HMPC meetings. Additional, topic based, meetings may be held electronically, as necessary.

5. Duration of activity

At its October 2010 meeting the Management Board agreed that following 18-24 months experience, and in the light of the work being undertaken by the ad hoc expert group, the status of the group would be reviewed. In March 2013 the Management Board agreed to extend the activity of the group for a further 2 years.

6. Rules of procedure

6.1. Responsibilities of the Chairperson and Vice Chairperson

The Chairperson, and in his/her absence the Vice Chairperson, is responsible for the efficient conduct of the business of the ad hoc expert group and shall in particular:

- Plan the work of the ad hoc expert group together with the Agency Secretariat;
- Monitor, together with the Agency 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 ad hoc expert group;
- Aim to achieve consensus on issues discussed by the ad hoc expert group;
- Decide, in exceptional cases, when a vote is necessary;
- Ensure, together with the ad hoc expert group and the Secretariat, the regulatory and scientific consistency of the Working Group's recommendations;
- Coordinate together with the Agency secretariat the work of this ad hoc expert group with that of the other relevant working parties of the Agency;
- Report on the activities of the ad hoc expert group to the CVMP, CHMP, working parties and HMPC as appropriate.

6.2. Election of Chairperson and Vice Chairperson

The Chairperson and Vice Chairperson of the ad-hoc expert group shall be elected by and from amongst the members of the group for a term of up to three years, which may be renewed.

6.3. Organisation of meetings and reporting arrangements

The ad hoc expert group shall meet regularly at the Agency.

The dates of meetings will be decided upon in consultation with members of the ad hoc expert group.

The meetings will be held and minuted in English.

The draft agenda for every meeting shall be circulated, together with the relevant documents, by the Agency Secretariat, in consultation with the chairperson, at least 14 calendar days before the meeting.

When a member of the ad hoc expert group is unable to participate at a meeting, part of meeting, or discussion topic due to conflict of interest, he/she must inform the Secretariat in advance in writing.

The ad hoc expert group may identify and propose topics for its consideration.

Any recommendation from the ad hoc expert group shall be transmitted to the Committees (CVMP, CHMP) for adoption.

When considered appropriate by the ad hoc expert group, oral presentations by third parties can be made during meetings of the group on matters directly related to the activities of the ad hoc expert group, following agreement of CVMP, CHMP.

The ad hoc expert group shall prepare a work plan for adoption by CVMP and HMPC which shall include topics identified and proposed by the group and any specific tasks identified by the Committees. The work plan shall be regularly reviewed and updated as necessary with the agreement of the CVMP and CHMP.

Agendas and minutes of the meetings of the ad hoc expert group shall be circulated to CVMP and CHMP.

The Chairperson will be invited to attend plenary meetings of CVMP and CHMP to report on the activities of the ad hoc expert group and ensure liaison with the work of the Committees.

The terms of reference and objectives of the ad hoc expert group shall be agreed by CVMP and CHMP.

6.4. Drafting Groups

When further consideration is required in order to prepare proposals on specific topics the ad hoc expert group may convene drafting groups constituted of members of the ad hoc expert group or experts, as appropriate. Drafting group meetings will take place electronically.

The drafting group will report to the ad hoc expert group.

6.5. Participation of Experts in meetings

A registry of 3Rs experts will be created and maintained by the Agency.

Invitation of additional experts is made on a case-by-case basis according to the expertise required to provide advice on the topics under discussion.

6.6. Guarantees of independence

The members of the ad hoc expert group 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 Agency, which is accessible to the public, on request at the Agency's office.

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

The specific provisions for handling declarations of interests and confidentiality undertakings as defined in the European Medicines Agency policy on the handling of conflicts of interests of Scientific Committee members and Experts, adopted by the Management Board (EMEA/613708/2010) are applicable to members of the ad hoc expert group and experts participating in the activities of the ad hoc expert group.

6.7. Code of conduct

Members of the ad hoc expert group and experts participating in the Agency's activities shall abide by the principles set out in the Agency's Code of Conduct.

6.8. European Medicines Agency Secretariat

Under the authority of the Executive Director, the Agency secretariat shall provide technical, Scientific and administrative support to the ad hoc expert group. This includes the following:

- Provide technical and scientific support to rapporteurs, and other members of the ad hoc expert group;
- Provide legal, regulatory and scientific support to the ad hoc expert group;
- Prepare and coordinate the work of the ad hoc expert group in consultation with the chairperson;
- Organise meetings of the ad hoc expert group ensuring timely circulation of meeting documents;
- Facilitate the necessary contacts between the ad hoc expert group and CVMP and CHMP;
- Ensure adequate coordination of the work carried out within the ad hoc expert group, CVMP, 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 ad hoc expert group in cooperation with the Chairperson;
- Prepare the agenda and minutes of the meetings of the ad-hoc expert group in consultation with the Chairperson;
- Communicate, when necessary, any CVMP, CHMP recommendations relevant to the ad hoc expert group to interested parties;
- Contribute to the identification of experts

The Executive Director of the Agency, members of the Agency secretariat, and representatives of the Commission, may attend all meetings of the ad hoc expert group.

6.9. Contacts with Interested Parties

Where relevant, the ad hoc expert group will establish contacts, on an advisory basis, with parties concerned with the development and implementation of 3Rs approaches.

Draft guidance documents and general regulatory developments will be subject to public consultation of all interested parties.

When considered appropriate by the ad hoc expert group, oral presentations by interested parties can be made during ad hoc expert group meetings in earlier stages of development of documents. The ad

hoc expert group may also meet with interested parties to discuss general matters or specific scientific issues with the agreement of the CVMP and CHMP.

In any case, the ad hoc expert group shall neither conduct any deliberations nor reach any formal decisions in the presence of members of interested parties.

Before any consultation session, interested party representatives and ad hoc expert group members will communicate to the Agency secretariat the points they would like to be discussed, so that an agenda of the session can be prepared for agreement by the ad hoc expert group Chairperson and circulation by the Agency secretariat.

6.10. General Provisions

The Members of the ad hoc expert group 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.

When participating in international or other *fora* on behalf of the CVMP and/or CHMP, members shall ensure the views expressed are those of the relevant committee.

When participating in international or other *fora* not specifically on behalf of the CVMP and/or CHMP, members shall make clear that the views expressed are their own views and not those of the committee.