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Committee for Medicinal Products for Human Use (CHMP)
Committee for Medicinal Products for Veterinary Use (CVMP)

# Mandate, objectives and rules of procedure for the joint CVMP/CHMP working group on the application of the 3Rs (replacement, reduction and refinement) in regulatory testing of medicinal products (J3RsWG)

## 1. General considerations

The Committee for Medicinal Products for Veterinary Use (CVMP) and the Committee for Medicinal Products for Human Use (CHMP) Rules of Procedures (EMEA/CVMP/422/04-Rev.1, EMEA/MB/47098/2007, EMEA/45110/2007, EMEA/MB/87146/2007 respectively) 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, the joint CVMP/CHMP expert group on the application of the 3Rs (JEG 3Rs) 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 European Medicines Agency (EMA) Management Board endorsed the formation of a joint expert group on the application of 3Rs in the development of medicinal products (JEG 3Rs), for an initial term of 2 years. At its March 2013 meeting the EMA Management Board endorsed the group's continued activity for an additional 2 years. A further 2 year extension was endorsed at the October 2014 meeting of the EMA Management Board. As the issues relating to the 3Rs concern both veterinary and human medicines it was considered appropriate that the group focussing on this area should be a joint CVMP/CHMP group.

In 2016 a review of the work of JEG 3Rs identified a number of initiatives that are expected to be largely completed by the end of its current mandate. As significant new projects have not been proposed, but recognising the continued importance of developments in 3Rs, it was agreed that the JEG 3Rs should be maintained but in a revised form with the creation of a Working Group (WG).

The new joint CVMP/CHMP working group on the application of the 3Rs (J3RsWG) is a smaller group more focused on reacting to requests from CHMP/CVMP, responding to public consultations of published guidance and reflection papers and preparing the final documents for adoption and

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continuing the scientific review of batch release tests for human and veterinary vaccines/biologicals for alignment with best practice in 3Rs.

It is recognised that much work is already being done in the 3Rs area by other European Commission bodies, particularly European Union Reference Laboratory for Alternatives to Animal Testing (EURL ECVAM) and European organisations such as the Council of Europe's European Directorate for the Quality of Medicines and Healthcare (EDQM); therefore, it is important to ensure that the Agency's group should complement and not duplicate their work.

## 2. Mandate 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 on the protection of animals used for scientific purposes.
- Foster strong ties with EDQM and European Commission (e.g. EURL ECVAM).
- Contributing to the development of guidelines and reflection papers in which 3Rs issues are applicable in collaboration with relevant working parties (WP).
- 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 International Cooperation on Harmonisation of Technical Requirements for registration of Pharmaceuticals for Human Use (ICH), and Veterinary Medicinal products (VICH), etc.

Since 2013, the JEG 3Rs has focused particularly 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.

For the period of 2017 to 2019 the tasks of J3RsWG remain unchanged although the focus is in the following areas:

(1) Finalisation and adoption of reflection papers and guidelines under development on 3Rs.

(2) 3Rs issues related to batch release testing for veterinary IVMPs and human vaccines & biologicals.

(3) Supporting implementation of Directive 2010/63/EU.

More detail on the specific projects in which the J3RsWG is actively involved will be provided in the Work plan.

## 3. Drafting groups

When further consideration is required in order to prepare proposals on specific topics the J3RsWG may convene drafting groups constituted of members of the J3RsWG or experts, as appropriate. Drafting group meetings will take place electronically and the output will be provided to the J3RsWG.

## 4. Composition and rules of participation

- The core of the J3RsWG consists of experts nominated by the relevant working parties and will be complemented, as necessary, by specified experts. Relevant core-working parties are considered to be the CHMP Safety Working Party (SWP-H), CHMP Biologicals Working Party (BWP), CVMP Safety Working Party (SWP-V), CVMP Efficacy Working Party (EWP), and Immunologicals Working Party (IWP). All J3RsWG members are included in the EMA European Experts list.
- In order to ensure that the objectives of the J3RsWG 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.
- Membership of the core-group is made up of one member from the Committees' working parties named above.
- CVMP and/or CHMP may nominate one of their members to act as a core-member of the group.
- Non-core working parties (CHMP Vaccines Working Party (VWP), CHMP Biosimilar medicinal products working party (BMWP) and the joint CHMP/CVMP Quality Working Party (QWP)) will nominate a contact point for 3Rs activities for J3RsWG. The contact point will provide information when requested to support the work of J3RsWG and apprise the respective WP of any 3Rs issue identified by J3RsWG.
- Other Committees will be included in J3RsWG activities and consultations when relevant, such as the Committee on Herbal Medicinal Products (HMPC), the Committee for Advanced Therapies (CAT) or the Paediatric Committee (PDCO).
- The nominated contact will be invited to attend the annual J3RsWG meeting if there is an item on the agenda relevant to their respective WP.
- EDQM and EURL ECVAM are invited to send a representative each to the meetings to act as observers and to any drafting group or specific 3Rs topic meeting organised to address particular 3Rs issue during the mandate of the WG.
- Co-opted experts may be invited to join the core-group when a specific need for additional expertise in the area of 3Rs to facilitate the work of the group has been identified. Representatives of European Commission's Directorate General for Health and Food Safety (DG SANTE) and DG Environment (contact point for National Competent Authorities for 2010/63/EU) may also be invited to attend meetings as observers in order to facilitate discussions relating to Directive 2010/63/EU or other applicable legislation, policy or strategy on 3Rs.
- 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 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 candidate countries for EU accession may participate with the agreement of the Chairperson and the Agency. Specific confidentiality rules will apply to observers.

# 5. Meeting frequency

The working group will generally meet once per year for a one day physical meeting.

Additional topic based meetings of the core-group will be held, as necessary.

Where the core-group considers that additional physical J3RsWG meetings are required, this will be specified in the work plan or specific endorsement obtained from CHMP/CVMP and EMA.

One of the main characteristics of the regular work of J3RsWG should be based in the use of IT facilities in order to improve efficiency and minimise costs. Use of tools such as tele/videoconference (including Adobe connect) should ensure the ability of J3RsWG to hold dynamic discussions, keeping members properly involved and replying to CHMP, CVMP, other Committees, Scientific Advice Working Party (SAWP) or other WP requests in a timely basis.

# 6. Duration of activity

In 2017, the Management Leadership Team endorsed the continuation of the working group for 3Rs with a three year mandate.

# 7. Rules of procedure

## *7.1. 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 J3RsWG and shall in particular:

- Plan the work of J3RsWG together with the Secretariat;
- Monitor, together with the 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 J3RsWG;
- Liaise with the Consistency Group regarding the guidelines produced by the J3RsWG;
- Aim to achieve consensus on issues discussed by J3RsWG;
- Decide, in exceptional cases, when a vote is necessary;
- Ensure, together with the J3RsWG and the Secretariat, the regulatory and scientific consistency of the working group's recommendations;

- Coordinate together with the Secretariat the work of this J3RsWG with that of the other relevant working parties of the Agency;
- Report on the activities of the J3RsWG to the CVMP, CHMP and working parties, as appropriate.

## *7.2. Election of Chairperson and Vice Chairperson*

The Chairperson and Vice Chairperson of the working group shall be chosen by and from amongst the members of J3RsWG including any co-opted members for a term of up to three years. A Committee member or an alternate may be also appointed by the Committee(s) to fulfil this responsibility

The Chairperson and Vice Chairperson shall be elected by the CHMP and then subject to the approval of the CVMP or vive-versa depending on the origin of the nominated Chairperson(s). Their appointment shall be for a term of three years which may be renewed once, subject to the renewal of the Mandate.

Regardless of the time of election of the Chairperson (s), he/she shall be appointed for a term of three years. This appointment may be renewed once.

Nominations should be submitted in writing to the EMA Secretariat of the working group. Candidates shall submit a brief résumé in support of their candidature at the time of the nomination.

### 7.2.1. Election or nomination of members

Core members from relevant working parties would be nominated by their working parties to act as a member of J3RsWG.

Non-core members will act as contact points to liaise with J3RsWG.

### 7.2.2. 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.

## *7.3. Organisation of meetings and reporting arrangements*

The J3RsWG would meet on an annual basis and produce an annual report of its work.

The dates of meetings will be decided upon in consultation with members of J3RsWG.

The meetings will be held and minutes written in English.

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

When a member of J3RsWG 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.

Any recommendation from J3RsWG shall be transmitted to the Committees (CVMP, CHMP) for adoption.

When considered appropriate by J3RsWG, oral presentations by third parties can be made during meetings of the group on matters directly related to the activities of J3RsWG, following agreement of CVMP, CHMP.

The J3RsWG shall prepare a work plan for adoption by CVMP and CHMP 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 J3RsWG 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 working group and ensure liaison with the work of the Committees.

The mandate and objectives of J3RsWG shall be agreed by CVMP and CHMP.

### *7.4. Guarantees of independence*

The members of J3RsWG 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 J3RsWG 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 declarations of interests for CVMP members and experts, adopted by the Management Board (EMEA/626261/2014) are applicable to members of the J3RsWG and experts participating in the activities of the J3RsWG.

### *7.5. Code of conduct*

Members of the working parties and experts participating in the EMA's activities shall abide by the principles set out in the European Medicines Agency Code of Conduct (EMA/385894/2012).

## 8. Agency Secretariat

Under the authority of the Executive Director, the Secretariat shall provide technical, scientific and administrative support to J3RsWG. This includes the following:

- Provide technical and scientific support to rapporteurs, and other members of J3RsWG;
- Provide legal, regulatory and scientific support to J3RsWG;
- Prepare and coordinate the work of J3RsWG in consultation with the Chairperson;
- Organise meetings of J3RsWG ensuring timely circulation of meeting documents;
- Facilitate the necessary contacts between J3RsWG and CVMP and CHMP;
- Ensure adequate coordination of the work carried out within J3RsWG, 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 J3RsWG in cooperation with the Chairperson;
- Prepare the agenda and minutes of the meetings of the working group in consultation with the Chairperson;
- Communicate, when necessary, any CVMP, CHMP recommendations relevant to J3RsWG to interested parties; and
- Contribute to the identification of experts.

The Executive Director of the Agency, members of the Secretariat, and representatives of the European Commission, may attend all meetings of J3RsWG.

## 9. Relationship with other WPs, committees and groups

See section 4 (Composition and rules of participation) for interaction between J3RsWG members and CHMP/CVMP WPs and observers from EURL ECVAM and EDQM.

## 10. General Provisions

The Members of J3RsWG 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.

## 11. Contacts with Interested Parties

Where relevant, J3RsWG 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 J3RsWG, oral presentations by interested parties can be made during J3RsWG meetings in earlier stages of development of documents. J3RsWG 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, J3RsWG 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 J3RsWG members will communicate to the Secretariat the points they would like to be discussed, so that an agenda of the session can be prepared for agreement by J3RsWG Chairperson and circulation by the Secretariat.