EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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

Concept paper on review and update of EMA guidelines to implement best practice with regard to 3Rs (replacement, reduction and refinement) in regulatory testing of medicinal products

Agreed by JEG 3Rs	October 2013
Adopted by CVMP for release for consultation	12 December 2013
Adopted by CHMP for release for consultation	19 December 2013
Start of public consultation	7 February 2014
End of consultation (deadline for comments)	31 May 2014

Comments should be provided using this template. The completed comments form should be sent to JEG-3Rs@ema.europa.eu

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1. Introduction

The Joint CHMP/CVMP ad-hoc expert group on the application of the 3Rs in the regulatory testing of medicinal products (JEG 3Rs), in coordination with relevant CHMP and CVMP working parties, has been reviewing existing EMA guidance documents with a view to ensuring that these reflect current best practice with regard to implementation of 3Rs approaches. In light of the work undertaken so far it seems likely that revisions to some guidelines may be warranted.

2. Problem statement

As science develops it is inevitable that some regulatory tests that were previously recommended will be superseded as a result of availability of new methodologies or will become redundant. There is a need to ensure that developments relevant to animal testing are reflected by corresponding updates to guidelines, and that guidelines do not include requirements and recommendations for unnecessary animal testing.

3. Discussion (on the problem statement)

In general, where scientific developments have led to amendments to tests, EMA guidelines have been updated to reflect these changes. However, following the creation of the JEG 3Rs, and in line with Directive 2010/63/EU, it is considered that it is an appropriate time to carry out a general review of EMA guidance documents with the aim of ensuring best practice in the implementation of 3Rs in the regulatory testing of medicinal products. Guidelines reviewed will be those overseen by the CHMP and CVMP Safety Working Parties (SWP), the CHMP Biologicals Working Party (BWP), the CHMP Vaccines Working Party (VWP), the CVMP Immunologicals Working Party (IWP), the joint CHMP/CVMP Quality Working Party (QWP) and the CVMP Efficacy Working Party (EWP). A preliminary review suggests that the number of guidelines affected will be relatively small.

With relevance to the EMA's work on this topic, it should be highlighted that Directives 2001/82/EC and 2001/83/EC require that animal testing should be conducted in accordance with Directive 86/609/EEC, now superseded by Directive 2010/63/EU. While the EMA and its scientific committees are not the bodies responsible for implementing Directive 2010/63/EU, they support the goals of the directive and will continue to play a role in eliminating repetitious and unnecessary animal testing.

While updates to some guidelines may be straight forward and uncontroversial, it can be expected that others will require considerable discussion and may only follow on from changes to other publications, most notably the European Pharmacopoeia. Individual updated guidelines will therefore be published as they are ready rather than together as a group.

As guidelines are updated it is intended that a statement highlighting the need to consider 3Rs will be included in each. However, guidelines will not be updated solely for the purpose of adding this statement.

4. Recommendation

The JEG 3Rs recommends that, in coordination with relevant CHMP and CVMP Working Parties, there should be a review of those EMA guidance documents which include reference to animal tests. This review will be limited to those guidance documents in force at the time of publication of this concept

paper. Where guidance documents are found not to reflect best practice with regards to the application of 3Rs, these should be updated or a plan for their update established.

The scope of the review will be limited to changes that relate to the implementation of 3Rs approaches. The aim will not be to open up guidelines for full revision.

5. Proposed timetable

February 2014:	Concept Paper to be released for consultation
31 May 2014:	Deadline for receipt of comments on the concept paper
From June 2014:	Review and update of relevant guidelines, with adoption of revised guidelines or update plans in parallel

6. Resource requirements for preparation

For the review of the guidelines 8 JEG 3Rs rapporteurs will be needed: one each from CHMP SWP, CVMP SWP, CHMP BWP, CHMP VWP, CVMP IWP and CVMP EWP, and two (one for human and one for veterinary medicinal products) from QWP. As well as the discussions in the JEG 3Rs, there will need to be corresponding discussions in the relevant CHMP/CVMP Working Parties.

The resource requirements for the revision of the guidelines will depend on the number of guidelines that need to be revised but could potentially involve the same number of rapporteurs as outlined in the previous paragraph. Any revision to a guideline will need to be overseen by the relevant CHMP/CVMP Working Party.

7. Impact assessment (anticipated)

The update of guidelines with a view to implementing best practice with regard to 3Rs will help to avoid confusion for both applicants and assessors and will facilitate compliance with Directive 2010/63/EU. It is noted that compliance with Directive 2010/63 may have resource implications for industry and regulatory authorities, for example if product specific validation of a 3Rs method is required.

8. Interested parties

Regulatory authorities for medicinal products for human and veterinary use, the human and veterinary pharmaceuticals industry, animal welfare bodies.

9. References to literature, guidelines, etc.

Directive 2001/83/EC of the European Parliament and of the Council, available at http://ec.europa.eu/health/documents/eudralex/vol-1/index_en.htm

Directive 2001/82/EC of the European Parliament and of the Council, available at http://ec.europa.eu/health/documents/eudralex/vol-5/index_en.htm

Directive 2010/63/EU of the European Parliament and of the Council, available at http://ec.europa.eu/environment/chemicals/lab_animals/home_en.htm