EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Medicinal Products for Human Use (CHMP)

Concept paper on the revision of the guideline on similar biological medicinal product

Agreed by BMWP and BWP	October 2011
Adoption by CHMP for release for consultation	17 November 2011
End of consultation (deadline for comments)	29 February 2012

The proposed guideline will replace the guideline on Similar Biological Medicinal Products (CHMP/437/04).

Comments should be provided using this template. The completed comments form should be sent to BMWP.Secretariat@ema.europa.eu

Keywords	*Similar biological medicinal product, biosimilar, biosimilarity exercise, comparability*

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1. Introduction

The so-called "overarching" guideline on similar biological (biosimilar) medicinal products CHMP/437/04 was discussed in CHMP in 2004 and, after external consultation, came into force in 2005. Reference to this guideline is implicit in the legislation where it is stated in Section 4, Part II, Annex I to Directive 2001/83/EC that *'the general principles to be applied [for similar biological medicinal products] are addressed in a guideline taking into account the characteristics of the concerned biological medicinal product published by the Agency'.*

The purpose of this guideline was:

- To introduce the concept of similar biological medicinal products;
- To outline the basic principles to be applied;
- To provide applicants with a 'user guide', showing where to find relevant scientific information in the various CHMP guidelines, in order to substantiate the claim of similarity.

Since 2005, the CHMP has seen numerous Scientific Advice procedures and Marketing Authorisation Applications, and several biosimilars have already been marketed. Thus, considerable experience has been gained on the concept of biosimilarity not only from a conceptual but also from a data perspective.

2. Problem statement

The CHMP considers that, following the principle that guidance documents should be regularly reviewed, the "overarching" guideline for biosimilars should be revisited in light of how biosimilars are currently being developed by Applicants, and should explain the concept around biosimilars, where necessary, in a clearer way. More specifically, the following (non-exhaustive) list of issues for further consideration have been identified:

- The principles of biosimilarity may have to be explained in a clearer way.
- Numerous terms are in use for "biosimilar" or "similar biological medicinal product", and often the term "biosimilar" has been used in an inappropriate way.
- Discuss the feasibility to follow the generic legal basis for some biological products.
- Some more specific aspects require re-discussion and potentially a refinement.

3. Discussion (on the problem statement)

The biosimilarity exercise follows the main concept that clinical benefit has already been established by the reference medicinal product, and that the aim of a biosimilar development programme is to establish similarity to the reference product, not clinical benefit. It may be of benefit to amend the guideline accordingly to make this principle, and its consequences, clearer to the reader.

Numerous terms are in use for "biosimilar" or "similar biological medicinal product", and often the term "biosimilar" has been used in an inappropriate way. It may therefore be prudent to discuss if a definition of "biosimilar", in extension of what is in the legislation and relevant CHMP guidance, is necessary.

As regards more specific aspects, there are some items in the current text that require refinement, e.g.

- A discussion of equivalence of efficacy and safety aspects, should this be necessary and not be covered by the revision of the general non-clinical and clinical guideline;
- There is mention of pharmaceutical form, strength and route of administration which should be the same for biosimilar and reference medicinal product. The current text specifies if these are not the same then there should be additional data in the context of a comparability exercise. It has to be reviewed if such a scenario is at all possible for a biosimilar.
- The current guideline gives a long collection of guideline references, including outdated ones. It should be discussed if this is useful and feasible, given the fact that many more guidelines have meanwhile been drafted. Consideration should be given if the scope of the document should move away from this particular aspect.

Article 10(4) of the Directive 2001/83/EC states '*Where a biological medicinal product which is similar to a reference biological product does not meet the conditions in the definition of generic medicinal products, owing to, in particular, differences relating to raw materials or differences in manufacturing processes of the biological medicinal product and the reference biological medicinal product, the results of appropriate pre-clinical tests or clinical trials relating to these conditions must be provided. The type and quantity of supplementary data to be provided must comply with the relevant criteria stated in the Annex and the related detailed guidelines. The results of other tests and trials from the reference medicinal product's dossier shall not be provided'.* Discussion is needed to clarify if in exceptional situations, e.g. where a very simple biological fully characterised on the quality level, a biological medicinal product could be authorised based on a bioequivalence study only combined with an extensive quality comparability exercise.

4. Recommendation

It is recommended to review the guideline on Similar Biological Medicinal Product ("overarching guideline") in light of experience gained and to propose changes where necessary.

5. Proposed timetable

Release for external consultation: November 2011

Deadline for external comments: February 2011

It is anticipated that the draft revised guideline will be released for consultation in the first semester of 2012.

6. Resource requirements for preparation

Experts from BMWP and BWP will develop the revision of the guideline in consultation with other CHMP working parties. At least one formal meeting of the drafting group will be required in the margins of the working party meetings.

7. Impact assessment (anticipated)

Anticipated benefit for industry and assessors of biosimilar products.

8. Interested parties

- Competent authorities of the member states
- Pharmaceutical industry

9. References to literature, guidelines, etc.

N/A