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**COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
(CHMP)**

**CONCEPT PAPER ON THE NEED FOR REVISION OF THE POINTS TO CONSIDER ON
THE CLINICAL INVESTIGATION OF MEDICINAL PRODUCTS OTHER THAN NSAIDS
IN RHEUMATOID ARTHRITIS (CPMP/EWP/556/95 REV. 1)**

AGREED BY EWP	January 2010
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Comments should be provided using this [template](#) to EWPSecretariat@ema.europa.eu

KEYWORDS	<i>Rheumatoid arthritis (RA), disease-modifying antirheumatic drugs (DMARD), symptom and structure modification, efficacy variables, endpoints, study design, comparator, early disease</i>
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1. INTRODUCTION

Since 2003 this guideline has presented guidance for the clinical development of slow-acting anti-rheumatic medicinal products aiming at symptom- and/or structure-modification (*e.g.* DMARDs, biologics) for the treatment of rheumatoid arthritis (RA). In the last years efforts have been made in that field with regard to the development of new products with an improved efficacy profile and novel insights have been gained with respect to the assessment of disease activity, joint damage and disability. Furthermore, new treatment strategies have been established which relate to early therapy, tight control and rapid switching of medication. Accordingly, new EULAR/ACR recommendations have been developed. Therefore several important additions and changes are needed to express the current state of scientific knowledge in this guideline.

2. PROBLEM STATEMENT

The search for improved and meaningful endpoints and study designs adapted to the changed pharmacologic profile of new agents and elaborated treatment strategies has prompted several groups of scientists to develop new recommendations for conducting clinical studies in RA. A need is identified to update the regulatory guidance on the clinical development of medicinal products intended for the treatment of RA.

3. DISCUSSION (ON THE PROBLEM STATEMENT)

The main topics to be discussed when revising the guidance document are:

1. New efficacy variables to assess clinical responses considering the improved efficacy of new biologic agents (*e.g.* (ACR70 response, Disease Activity Score [DAS] remission, and physical function by the Health Assessment Questionnaire [HAQ])) according to the claimed therapeutic indication.
2. Developments in the assessment of structural damage
3. Developments in the assessments of QoL
4. Primary endpoints (alternatives to the ACR 20/50/70% response rates).
5. Choice of comparators including Placebo control for first, second and third line indication.
6. Biologic agents as active comparators.
7. Duration of studies necessary for intended claims of symptom modifying effect, disease modifying effect or for a claim to delay progression of structural damage.
8. Duration of placebo-controlled phase.
9. New study designs (*e.g.* add on, switching, drug free intervals).
10. Study populations: *e.g.* severe RA, early RA, undifferentiated arthritis (and to look at how accurately biomarkers really reflect prognosis)
11. Concept of traditional versus new potential claims.
12. New safety aspects.

4. RECOMMENDATION

It is proposed to revise the current CHMP Points to Consider (PtC) addressing the clinical investigation of medicinal products other than NSAIDs for treatment of RA in order to achieve a European common position on the above-mentioned issues.

5. PROPOSED TIMETABLE

It is anticipated that a new draft CHMP guideline may be available in the 2nd/3rd Quarter 2010 to be later released for 6 months for external consultation and, thereafter, finalised within 6 months.

6. RESOURCE REQUIREMENTS FOR PREPARATION

The preparation of this revision of the guideline will involve the EWP. It is anticipated that at least one plenary session discussions at the EWP will be needed.

7. IMPACT ASSESSMENT (ANTICIPATED)

The revision of the PtC on clinical investigation of medicinal products other than NSAIDs in RA will be helpful to achieve consensus in the evaluation of such products by regulatory authorities. Furthermore, it is expected that such guidance document would improve quality and comparability of submitted studies by pharmaceutical industries.

8. INTERESTED PARTIES

It is envisioned to contact EULAR (European League Against Rheumatism) and GREES (Group for the Respect of Ethics and Excellence in Science).

9. REFERENCES TO LITERATURE, GUIDELINES ETC

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