



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

**CONCEPT PAPER ON A
GUIDELINE ON THE CHEMICAL AND PHARMACEUTICAL QUALITY
DOCUMENTATION CONCERNING BIOLOGICAL INVESTIGATIONAL MEDICINAL
PRODUCTS IN CLINICAL TRIALS**

AGREED BY BWP	13 February 2008
ADOPTION BY CHMP FOR RELEASE FOR CONSULTATION	21 February 2008 ¹
END OF CONSULTATION (DEADLINE FOR COMMENTS)	31 May 2008 ²

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¹ Last day of relevant CHMP meeting

² Last day of the month concerned

1. INTRODUCTION AND PROBLEM STATEMENT

Clinical trials within the EU are regulated by Directive 2001/20/EC (1) which came into force in May 2004. As a consequence all Member States require that a documentation supporting an adequate quality for investigational medicinal products has to be submitted to the competent authority of the respective Member State. Approval of trials is the responsibility of individual Member States, who are evaluating the products used in clinical studies.

Some Member States have developed requirements for the quality part of a request for authorisation of the clinical trials. However, clinical trials are often designed as multi-centre studies potentially involving different Member states and for the sake of consistency and transparency it is of great importance to ensure harmonised requirements for the documentation to be submitted throughout the European Community. Furthermore a clear differentiation between the requirements for a dossier for a clinical trial application (IMPD) and a dossier for a marketing authorisation application is needed. Quality requirements for an investigational medicinal product should clearly address safety aspects and should consider the nature of the product, the state of development/clinical phase, patient population, nature and severity of the illness as well as type and duration of the clinical trial itself.

Assuring the quality of medicinal products of biological origin is a complex process. A reliable assessment of quality is critical for weighing the foreseeable risks against the anticipated benefits for trial subjects on which the decision for approving clinical trials is based. Current guidance on the quality of biological/ biotechnological medicinal products is found in guidelines pertinent to biological/biotechnology medicinal products. Most of these guidelines do not provide appropriate guidance for products in development, either prior to or during clinical trials; rather they are directed towards data requirements for marketing authorisation applications. A guideline on virus safety (3) giving advice on the requirements for viral safety of investigational medicinal products is under preparation. For material of non-biological origin a guideline (4) on quality requirements is already available.

In view of the current lack of common reference guidance on which to base the assessment of quality of biological clinical trial material and the difference in experience among sponsors and competent authorities, there is a need to promote a harmonised approach throughout the European Union and facilitate multi-centre clinical trials in particular. The need for guidance in this area has been recognised by regulators and the Industry. Consequently, it is proposed to develop a new guideline with the title "GUIDELINE ON THE CHEMICAL AND PHARMACEUTICAL QUALITY DOCUMENTATION CONCERNING BIOLOGICAL INVESTIGATIONAL MEDICINAL PRODUCTS IN CLINICAL TRIALS"

2. DISCUSSION AND RECOMMENDATION

Although guidance would be beneficial for a wide range of biological products, it is proposed to limit the scope of the guideline initially to biological/biotechnology products in order to provide the most specific guidance possible in this area for regulators and for the Industry. Thus the guideline should mainly apply to proteins and polypeptides, their derivatives, and products of which they are components (e.g. conjugates). These proteins and polypeptides are produced from recombinant or non-recombinant cell-culture expression systems and can be highly purified and characterized using an appropriate set of analytical procedures. The principles that will be outlined in the document may also apply to other biological products.

Taking account of existing guidance (2) established for submission of Marketing Authorisation Applications for biological/biotechnology products, the proposed guideline will address specific aspects relevant to products under development and should help to identify the essential quality requirements.

The guideline will address critical quality aspects including:

1. The extent of information needed about the structure of a molecule and the quality characteristics of the drug substance

2. Information needed on cell banks
3. The extent of characterisation needed for process and product related impurities
4. The extent of information needed on the manufacturing process, the control of critical steps and in-process controls
5. The extent of development and/or validation of the manufacturing process that is required prior to and during clinical development.
6. The extent of qualification/validation required for the analytical procedures
7. Setting and justification of preliminary specifications
8. The requirements for stability data
9. Changes that require a substantial amendment to a clinical trial application

3. PROPOSED TIMETABLE

It is aimed that a guideline for consultation can be adopted in 2009 by BWP/CHMP, followed by a 6-month consultation period.

4. RESOURCE REQUIREMENTS FOR PREPARATION

A drafting group has been formed, which will meet via teleconference as well as in the margins of the BWP meetings and at dedicated drafting group meetings of which at least four will be required.

5. IMPACT ASSESSMENT (ANTICIPATED)

The development of this Guideline is part of the ongoing general development of suitable quality standards. It will result in a more consistent assessment of applications for clinical trials by regulators, set clearer standards and expectations for industry, and therefore be helpful for a harmonised regulatory policy.

The relatively small resource implications for preparation of a Guideline are fully justified and are compensated by the fact that application of a Guideline will make assessment easier and will result in less resources being needed during assessment.

6. INTERESTED PARTIES

In the preparation of this guideline, the BWP will liaise and exchange experiences with experts from national authorities in charge of approval of clinical trials in Member States. Relevant CHMP working parties will be consulted as required. The draft guideline will be made publicly available to interested parties for a 6-month consultation period before finalisation.

7. REFERENCES TO LITERATURE, GUIDELINES ETC

1. Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use
2. European Guidelines on Quality and Biologicals (available on EMEA's Website: www.emea.europa.eu) and in particular:
 - Draft Guideline on Virus Safety Evaluation of Biotechnological Investigational Medicinal Products (EMEA/CHMP/BWP/398498/2005)
 - Guideline on the Requirements to Chemical and Pharmaceutical Quality Documentation Concerning Investigational Medicinal products in Clinical Trials (CHMP/QWP/185401/2004)